SECRETED POLYPEPTIDE SPECIES AND USE THEREOF

FIELD OF THE INVENTION

The invention relates to polypeptide species secreted in human plasma, isolated polynucleotides encoding such polypeptides, polymorphic variants thereof, and the use of said nucleic acids and polypeptides or compositions thereof for detection assays and disease diagnosis and medical treatment.

BACKGROUND

The non-specific nature of many disease symptoms often makes definitive diagnosis difficult for medical practitioners. Patient descriptions are often variable or inaccurate. More quantitative diagnostic methods suffer from variability, both between individuals and between readings on a single individual. Thus, diagnostic measures must be standardized and applied to individuals with well-documented and extensive medical histories. Even with these controls, symptoms for entirely different underlying conditions can appear identical. In addition, many serious conditions result from a combination of factors, such as neuropsychiatric diseases (e.g., schizophrenia and bipolar disease, see Johnston-Wilson, et al., Int J Neuropsychopharmacol, 2001, 4:83-92) and metabolic disorders (e.g., diabetes, see Gloyn and McCarthy, Best Pract Res Clin Endocrinol Metab, 2001, 15:293-308). Current diagnostic methods often do not reveal the underlying cause(s) for a given observation or reading. Therefore, a therapeutic strategy based on a particular positive result likely will not address the causative problem and may even be harmful to the individual.

Methods of diagnosis that rely on nucleotide detection include genetic approaches and expression profiling. For example, genes that are known to be involved in a particular disorder may be screened for mutations using common genotyping techniques such as sequencing, hybridization-based techniques, or PCR. In another example, expression from a known gene may be tracked by standard techniques including RTPCR, various hybridization-based techniques, and sequencing. These strategies often do not enable a practitioner to detect differences in mRNA processing and splicing, translation rate, mRNA stability, and posttranslational modifications such as proteolytic processing, phosphorylation, glycosylation, and amidation.

To address the current weaknesses in the diagnostic state of the art, the invention provides new information relating to the range of polypeptides that are found in human plasma. Human blood plasma is a most useful source of proteins associated with both health and disease. Plasma not only

contains active proteins and tell-tale disease markers; it may be obtained non-invasively in fairly large quantities from both patients and control subjects (as opposed to tissue, which is often difficult to obtain in large amounts from controls). Furthermore, blood, plasma, and serum are used quite generally for existing clinical tests (e.g., genomic approaches). However, many of the cells responsible for the protein content of plasma are not to be found in the blood, thus limiting genomic approaches. Finally, plasma is a fluid and therefore may be pooled (again, in contrast to tissue) to obtain a large and representative sample for analysis.

Analysis of the plasma proteome is challenging in view of the large numbers of proteins expected to be present and the wide dynamic range of concentrations, known to span at least 11 to 12 orders of magnitude. In order to identify and characterize polypeptides present at very low concentrations, it is necessary to start with a large sample volume to ensure a sufficient quantity for detection by mass spectrometry. For example, if 100 fmol of protein is required for successful separation, digestion, and mass spectrometric identification, then a protein concentration of at least 1 nM is required with a sample size of 100 µl. However, this required minimum concentration falls to 100 fM if one litre of sample is available.

The invention described herein stems from this logic. An industrial-scale (2.5L) method, involving sample pooling, is detailed for the analysis of smaller proteins (molecular weight less than about 40kD, and mostly under 20kD). Thousands of peptides resulting from polypeptides were identified from a single pool. As proof of concept for the methods of the invention, low abundance proteins such as leptin and ghrelin and peptides such as bradykinin, were clearly identified. This is the first time that the small proteins in human blood plasma have been analyzed so extensively. Thus, the invention discloses proteins that have not been previously found in blood plasma. By providing the actual plasma polypeptide species, differences in mRNA processing and splicing, translation rate, mRNA stability, and posttranslational modifications are revealed. Such posttranslational modifications (e.g., proteolytic processing, phosphorylation, glycosylation, and amidation) may, and often do, affect the function of a particular polypeptide. In addition, plasma localization points to a novel, previously unknown function for the polypeptides of the invention. These polypeptides are described as "Human Plasma Polypeptides" or HPPs. These polypeptide sequences are related to the polypeptides with accession numbers listed in Table 1 and include polypeptide species that comprise one or more of the amino acid sequences listed in Table 3.

The present invention discloses "Human Plasma Polypeptides" (HPPs), fragments, and post-translationally modified species of HPPs that are present in human plasma. The HPPs of the invention represent an important tool for diagnosis and drug development. HPPs are secreted factors and as

such, are easy to detect and target, e.g., with a detectable molecule, protein chip, or modulator.

SUMMARY OF THE INVENTION

The present invention is directed to compositions related to polypeptide species secreted in human plasma. These polypeptide species are designated herein "Human Plasma Polypeptides," or HPPs. Such Human Plasma Polypeptides comprise an amino acid sequence selected from the list of Table 3. Compositions include HPP precursors, antibodies specific for HPPs, including monoclonal antibodies and other binding compositions derived therefrom. Further included are methods of making and using these compositions. Precursors of the invention include unmodified precursors, proteolytic precursors of the group consisting of the sequences from Table 3, and intermediates resulting from alternative proteolytic sites in the group consisting of the sequences from Table 3.

A preferred embodiment of the invention includes HPPs having a posttranslational modification, such as a phosphorylation, glycosylation, acetylation, amidation, or a C-, N- or O-linked carbohydrate group. Additionally preferred are HPPs with intra- or inter-molecular interactions, e.g., disulfide and hydrogen bonds that result in higher order structures. Also preferred are HPPs that result from differential mRNA processing or splicing. Preferably, the HPPs represent posttranslationally modified species, structural variants, or splice variants that are present in plasma.

In another aspect, the invention includes HPPs comprising a sequence which is at least 95 percent identical to a sequence selected from the group of sequences listed in Table 3. Preferably, the invention includes polypeptides comprising at least 97 percent, and more preferably at least 98 percent, and still more preferably at least 99 percent, identity with any one of the sequences selected from Table 3. Most preferably, the invention includes polypeptides comprising a sequence at least 99 percent identical to a sequence selected from the group of sequences listed in Table 3.

In another aspect, the invention includes natural variants of HPPs having a frequency in a selected population of at least two percent. More preferably, such natural variant has a frequency in a selected population of at least five percent, and still more preferably, at least ten percent. Most preferably, such natural variant has a frequency in a selected population of at least twenty percent. The selected population may be any recognized population of study in the field of population genetics. Preferably, the selected population is Caucasian, Negroid, or Asian. More preferably, the selected population is French, German, English, Spanish, Swiss, Japanese, Chinese, Irish, Korean, Singaporean, Icelandic, North American, Israeli, Arab, Turkish, Greek, Italian, Polish, Pacific Islander, Finnish, Norwegian, Swedish, Estonian, Austrian, or Indian. More preferably, the selected population is Icelandic, Saami, Finnish, French of Caucasian ancestry, Swiss, Singaporean of Chinese

ancestry, Korean, Japanese, Quebecian, North American Pima Indians, Pennsylvanian Amish and Amish Mennonite, Newfoundlander, or Polynesian.

A preferred aspect of the invention provides a composition comprising an isolated HPP, i.e., an HPP free from proteins or protein isoforms having a significantly different isoelectric point or a significantly different apparent molecular weight from the HPP. The isoelectric point and molecular weight of an HPP may be indicated by affinity and size-based separation chromatography, 2-dimensional gel analysis, and mass spectrometry.

In an additional aspect, the invention includes modified HPPs. Such modifications include protecting/blocking groups, linkage to an antibody molecule or other cellular ligand, and detectable labels, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the protein. Chemical modifications may be carried out by known techniques, including but not limited, to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH4, acetylation, formylation, oxidation, reduction, or metabolic synthesis in the presence of tunicamycin.

Also provided by the invention are chemically modified derivatives of the polypeptides of the invention which may provide additional advantages such as increased solubility, stability and circulating time of the polypeptide, or decreased immunogenicity (e.g., water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol). The HPPs are modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three or more attached chemical moieties.

In another aspect, the invention includes polynucleotides encoding an HPP of the invention, polynucleotides encoding a polypeptide having an amino acid sequence selected from the group of sequences listed in Table 3, antisense oligonucleotides complementary to such sequences, oligonucleotides complementary to HPP gene sequences for diagnostic and analytical assays (e.g., PCR, hybridization-based techniques).

In another aspect, the invention provides a vector comprising DNA encoding an HPP. The invention also includes host cells and transgenic nonhuman animals comprising such a vector.

There is also provided a method of making an HPP or HPP precursor. One preferred method comprises the steps of (a) providing a host cell containing an expression vector as disclosed above; (b) culturing the host cell under conditions whereby the DNA segment is expressed; and (c) recovering the protein encoded by the DNA segment. Another preferred method comprises the steps of: (a) providing a host cell capable of expressing an HPP; (b) culturing said host cell under

conditions that allow expression of said HPP; and (c) recovering said HPP. Within one embodiment the expression vector further comprises a secretory signal sequence operably linked to the DNA segment, the cell secretes the protein into a culture medium, and the protein is recovered from the medium. An especially preferred method of making an HPP includes chemical synthesis using standard peptide synthesis techniques, as described in the section titled "Chemical Manufacture of HPP compositions" and in Example 2.

In another aspect, the invention includes isolated antibodies specific for any of the polypeptides, peptide fragments, or peptides described above. Preferably, the antibodies of the invention are monoclonal antibodies. Further preferred are antibodies that bind to an HPP specifically or exclusively, that is, antibodies that do not recognize other polypeptides with high affinity. Anti-HPP antibodies have purification, detection, diagnostic and prognostic applications. Preferred anti-HPP antibodies for purification and detection are attached to a label group. Detection methods include, but are not limited to, those that employ antibodies or antibody-derived compositions specific for an HPP antigen. A preferred detection method is an enzyme-linked immunosorption assay (ELISA). Compositions comprising one or more antibodies described above, together with a pharmaceutically acceptable carrier are also within the scope of the invention, e.g, for in vivo detection.

Detection methods for identifying HPPs in specific tissue samples and biological fluids (preferably plasma) form part of the invention. Detection methods for identifying HPP expression in cell-based samples are also included.

The invention further provides methods that comprise detecting the level of at least one HPP in a sample of body fluid, preferably blood plasma. Further included are methods of using HPP compositions, including primers complementary to HPP genes and/or messenger RNA and anti- HPP antibodies, for detecting and measuring quantities of HPPs in tissues and biological fluids, preferably plasma. In addition, the invention includes detection methods comprising mass spectrometry, retentate chromatography (including protein arrays), and surface enhanced laser desorption/ionization (SELDI) techniques. These methods are also suitable for clinical screening, prognosis, monitoring the results of therapy, identifying patients most likely to respond to a particular therapeutic treatment.

The invention provides kits that may be used in the above-recited methods and that may comprise single or multiple preparations, adsorbant and substrate materials, antibodies, label groups, other reagents, if needed, and directions for use. The kits may be used for diagnosis or for assays to identify new diagnostic agents.

In a preferred embodiment, detection of increased plasma levels of at least one HPP of the

invention indicates an increased risk of an HPP disorder associated with the increased HPP. Preferably, said detection indicates that an individual has at least a 1.05-fold, 1.1-fold, 1.15-fold, and more preferably at least a 1.2-fold increased likelihood of developing said HPP disorder. Alternatively, depending on the specific HPP, detection of decreased plasma levels of at least one HPP of the invention indicates that an individual has an increased risk of an HPP disorder associated with the increased HPP. The amount of HPP increase or decrease observed in an individual compared to a control sample will correlate with the certainty of the prediction. As individual plasman HPP levels will vary depending on family history and other risk factors, each will preferably be examined on a case-by-case basis. In preferred embodiments, HPP is detected in a human plasma sample by the methods of the invention. Especially preferred techniques are mass spectrometry, retentate chromatography (including protein arrays), and immunodetection. Preferably, a prediction or diagnosis is based on at least a 1.1-, 1.15-, 1.2-, 1.25-, and more preferably a 1.5-fold increase (resp. decrease) in the experimental HPP level as compared to the control.

Further aspects of the invention are also described in the specification and in the claims.

DETAILED DESCRIPTION OF THE INVENTION

The present invention described in detail below provides compositions, methods, and kits useful for screening and diagnosis of human plasma; for identifying individuals most likely to respond to a particular therapeutic treatment; and for monitoring the results of therapy. For clarity of disclosure, and not by way of limitation, the invention will be described with respect to the analysis of blood plasma samples. However, as one skilled in the art will appreciate, the assays and techniques described below can be applied to other biological fluid samples (e.g. cerebrospinal fluid, lymph, bile, plasma, saliva or urine) or tissue samples. The methods and compositions of the present invention are useful for screening, diagnosis and prognosis of a living individual, but may also be used for postmortem diagnosis in an individual.

Definitions

As used herein, the term "nucleic acids" and "nucleic acid molecule" is intended to include DNA molecules (e.g., cDNA or genomic DNA) and RNA molecules (e.g., mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA. Throughout the present specification, the expression "nucleotide sequence" may be employed to designate indifferently a polynucleotide or a nucleic acid. More precisely, the expression "nucleotide sequence" encompasses the nucleic material

itself and is thus not restricted to the sequence information (i.e. the succession of letters chosen among the four base letters) that biochemically characterizes a specific DNA or RNA molecule. Also, used interchangeably herein are terms "nucleic acids", "oligonucleotides", and "polynucleotides".

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences which naturally flank the nucleic acid (i.e., sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated HPP nucleic acid molecule can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized. Using all or a portion of the nucleic acid as a hybridization probe, HPP nucleic acid molecules can be isolated using standard hybridization and cloning techniques (e.g., as described in Sambrook, J., Fritsh, E. F., and Maniatis, T. Molecular Cloning. A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989).

As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively linked. Such vectors are referred to herein as "expression vectors". In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" can be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

As used herein, the term "hybridizes to" is intended to describe conditions for moderate

stringency or high stringency hybridization, preferably where the hybridization and washing conditions permit nucleotide sequences at least 60% homologous to each other to remain hybridized to each other. Preferably, the conditions are such that sequences at least about 70%, more preferably at least about 80%, even more preferably at least about 85%, 90%, 95% or 98% homologous to each other typically remain hybridized to each other. Stringent conditions are known to those skilled in the art and can be found in Current Protocols in Molecular Biology, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. In a preferred, non-limiting example, stringent hybridization conditions for nucleic acid interactions are as follows: the hybridization step is realized at 65°C in the presence of 6 x SSC buffer, 5 x Denhardt's solution, 0,5% SDS and 100µg/ml of salmon sperm DNA. The hybridization step is followed by four washing steps:

- two washings during 5 min, preferably at 65°C in a 2 x SSC and 0.1%SDS buffer;
- one washing during 30 min, preferably at 65°C in a 2 x SSC and 0.1% SDS buffer,
- one washing during 10 min, preferably at 65°C in a 0.1 x SSC and 0.1%SDS buffer,

these hybridization conditions being suitable for a nucleic acid molecule of about 20 nucleotides in length. It will be appreciated that the hybridization conditions described above are to be adapted according to the length of the desired nucleic acid, following techniques well known to the one skilled in the art, for example be adapted according to the teachings disclosed in Hames B.D. and Higgins S.J. (1985) Nucleic Acid Hybridization: A Practical Approach. Hames and Higgins Ed., IRL Press, Oxford; and Current Protocols in Molecular Biology.

"Percent homology" is used herein to refer to both nucleic acid sequences and amino acid sequences. Amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "homology". To determine the percent homology of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence and non-homologous sequences can be disregarded for comparison purposes). The length of a reference sequence aligned for comparison purposes is at least 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, and even more preferably at least 70%, 80%, 90% or 95% of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are homologous at that position. The percent homology between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % homology=# of identical positions/total # of positions 100).

The comparison of sequences and determination of percent homology between two sequences can be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Karlin and Altschul (1990) Proc. Natl. Acad. Sci. USA 87:2264-68, modified as in Karlin and Altschul (1993) Proc. Natl. Acad. Sci. USA 90:5873-77. Such an algorithm is incorporated into the NBLAST and XBLAST programs (version 2.0) of Altschul, et al. (1990) J. Mol. Biol. 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score=100, wordlength=12 to obtain nucleotide sequences homologous to the sequences of the invention. BLAST protein searches can be performed with the XBLAST program, score=50, wordlength=3 to obtain amino acid sequences homologous to the polypeptide sequences of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) Nucleic Acids Research 25(17):3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See http://www.ncbi.nlm.nih.gov. Another preferred, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller, CABIOS (1989). Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.

The term "polypeptide" refers to a polymer of amino acids without regard to the length of the polymer; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide. This term also does not specify or exclude post-translational modifications of polypeptides, for example, polypeptides which include the covalent attachment of glycosyl, acetyl, phosphate, amide, lipid, carboxyl, acyl, or carbohydrate groups are expressly encompassed by the term polypeptide. Also included within the definition are polypeptides which contain one or more analogs of an amino acid (including, for example, non-naturally occurring amino acids, amino acids which only occur naturally in an unrelated biological system, modified amino acids from mammalian systems etc.), polypeptides with substituted linkages, as well as other modifications known in the art, both naturally occurring and non-naturally occurring.

The term "protein" as used herein may be used synonymously with the term "polypeptide" or may refer to, in addition, a complex of two or more polypeptides which may be linked by bonds other than peptide bonds, for example, such polypeptides making up the protein may be linked by disulfide bonds. The term "protein" may also comprehend a family of polypeptides having identical amino

acid sequences but different post-translational modifications, particularly as may be added when such proteins are expressed in eukaryotic hosts.

An "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein of the invention (i.e., HPP or biologically active fragment thereof) is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of a protein according to the invention in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. In one embodiment, the language "substantially free of cellular material" includes preparations of a protein according to the invention having less than about 30% (by dry weight) of protein other than the protein of the invention (also referred to herein as a "contaminating protein"), more preferably less than about 20% of protein other than the protein according to the invention, still more preferably less than about 10% of protein other than the protein according to the invention, and most preferably less than about 5% of protein other than the protein according to the invention. When the protein according to the invention or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the protein preparation.

The language "substantially free of chemical precursors or other chemicals" includes preparations of a protein of the invention in which the protein is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of a protein of the invention having less than about 30% (by dry weight) of chemical precursors or non-protein chemicals, more preferably less than about 20% chemical precursors or non-protein chemicals, still more preferably less than about 10% chemical precursors or non-protein chemicals, and most preferably less than about 5% chemical precursors or non-protein chemicals.

The term "recombinant polypeptide" is used herein to refer to polypeptides that have been artificially designed and which comprise at least two polypeptide sequences that are not found as contiguous polypeptide sequences in their initial natural environment, or to refer to polypeptides which have been expressed from a recombinant polynucleotide.

"Plasma" is the liquid part of the blood and lymphatic fluid, comprising about half of the volume. Plasma is devoid of cells and, unlike serum, has not clotted. Blood plasma contains antibodies and other proteins. Blood collected from an individual is often subjected to centrifugation

to remove cellular components. Another method of plasma separation includes sterile filtration, as described in US Patent 6241886.

The term "Human Plasma Polypeptide" or "HPP" refers to a polypeptide comprising the sequence described by any one of the accession numbers listed in Table 1 or any amino acid sequence selected from the group consisting of the sequences from Table 3. Such polypeptide may be post-translationally modified as described herein. HPPs may also contain other structural or chemical modifications such as disulfide linkages or amino acid side chain interactions such as hydrogen and amide bonds that result in complex secondary or tertiary structures. HPPs also include mutant polypeptides, such as deletion, addition, swap, or truncation mutants, fusion polypeptides comprising such polypeptides, and polypeptide fragments of at least three, but preferably 8, 10, 12, 15, or 21 contiguous amino acids of the sequences of Table 3. Further included are HPP proteolytic precursors and intermediates of the sequence selected from the group consisting of the sequences from Table 3. The invention embodies polypeptides encoded by the nucleic acid sequences of HPP genes or HPP mRNA species, preferably human HPP genes and mRNA species, including isolated HPPs consisting of, consisting essentially of, or comprising the sequences from Table 3. Preferred HPPs retain at least one biological activity of HPPs from Table 3.

The term "biological activity" as used herein refers to any function carried out by an HPP. These include but are not limited to: (1) circulating through the bloodstream of human individuals; (2) antigenicity, or the ability to bind an anti-HPP specific antibody; (3) immunogenicity, or the ability to generate an anti-HPP specific antibody; and (4) interaction with an HPP target molecule or adsorbant.

An "HPP-related disorder" or "HPP-related disease" describes any medical condition known to be associated with an HPP of the invention. HPP-related disorders include conditions where the presence of an abnormal level of an HPP or HPP polynucleotide is indicative that an individual has or is at risk of developing that condition. HPP-related disorders also include conditions where the presence of an abnormal form of an HPP or HPP polynucleotide (e.g., due to mutation, truncation, increased or decreased biological activity, abnormal posttranslational modification or processing) is indicative that an individual has or is at risk of developing that condition.

Another aspect of the invention pertains to anti-HPP antibodies. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, i.e., molecules that contain an antigen-binding site which specifically binds (immunoreacts with) an antigen, such as HPP, or a biologically active fragment or homologue thereof. Preferred antibodies bind to an HPP exclusively and do not recognize other polypeptides with high affinity. Examples of immunologically active portions of immunoglobulin molecules include F(ab) and $F(ab')_2$

fragments which can be generated by treating the antibody with an enzyme such as pepsin. The invention provides polyclonal and monoclonal antibodies that bind an HPP, or a biologically active fragment or homologue thereof. The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen-binding site capable of immunoreacting with a particular epitope of an HPP. A monoclonal antibody composition thus typically displays a single binding affinity for a particular HPP with which it immunoreacts. Preferred HPP antibodies are attached to a label group.

As used herein, a "label group" is any compound that, when attached to a polynucleotide or polypeptide (including antibodies), allows for detection or purification of said polynucleotide or polypeptide. Label groups may be detected or purified directly or indirectly by a secondary compound, including an antibody specific for said label group. Useful label groups include radioisotopes (e.g., ^{32}P, ^{35}S, ^{3}H, ^{125}I), fluorescent compounds (e.g., 5-bromodesoxyuridin, umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride, phycoerythrin acetylaminofluorene, digoxigenin), luminescent compounds (e.g., luminol, GFP, luciferin, aequorin), enzymes or enzyme co-factor detectable labels (e.g., peroxidase, luciferase, alkaline phosphatase, galactosidase, or acetylcholinesterase), or compounds that are recognized by a secondary factor such as strepavidin, GST, or biotin. Preferably, a label group is attached to a polynucleotide or polypeptide in such a way as to not interfere with the biological activity of the polynucleotide or polypeptide.

Radioisotopes may be detected by direct counting of radioemission, film exposure, or by scintillation counting, for example. Enzymatic labels may be detected by determination of conversion of an appropriate substrate to product, usually causing a fluorescent reaction. Fluorescent and luminescent compounds and reactions may be detected by, e.g., radioemission, fluorescent microscopy, fluorescent activated cell sorting, or a luminometer.

"Adsorbent" refers to any material capable of adsorbing a polypeptide (i.e., an HPP). The term "adsorbent" is used herein to refer both to a single material ("monoplex adsorbent") (e.g., a compound or functional group) to which a polypeptide is exposed, and to a plurality of different materials ("multiplex adsorbent") to which a sample is exposed. The adsorbent materials in a multiplex adsorbent are referred to as "adsorbent species." For example, an addressable location on a substrate can comprise a multiplex adsorbent characterized by many different adsorbent species (e.g., anion exchange materials, metal chelators, or antibodies), having different binding characteristics. The basis of attraction is generally a function of chemical or biological molecular recognition. Bases for attraction between an adsorbent and a polypeptide include, for example, (1) a salt-promoted

interaction, e.g., hydrophobic interactions, thiophilic interactions, and immobilized dye interactions; (2) hydrogen bonding and/or van der Waals forces interactions and charge transfer interactions, such as in the case of a hydrophilic interactions; (3) electrostatic interactions, such as an ionic charge interaction, particularly positive or negative ionic charge interactions; (4) the ability of the polypeptide to form coordinate covalent bonds (i.e., coordination complex formation) with a metal ion on the adsorbent; (5) enzyme-active site binding; (6) reversible covalent interactions, for example, disulfide exchange interactions; (7) glycoprotein interactions; (8) biospecific interactions; or (9) combinations of two or more of the foregoing modes of interaction. That is, the adsorbent can exhibit two or more bases of attraction, and thus be known as a "mixed functionality" adsorbent.

HPPs of the invention

The Human Plasma Polypeptides (HPPs) of the invention are described in Table 1 and 3. HPPs comprising an amino acid sequence selected from the group consisting of the sequences from Table 3 and fragments thereof are secreted and circulate in blood plasma.

The HPPs of the invention are known polypeptides that have not previously been found in human plasma. Thus, the invention introduces a new role or function for these polypeptides. HPPs listed in Table 1 include polypeptide species that are not expected to be found in plasma, as described in Table 1.

The terms "Human Plasma Polypeptide" and "HPP" are used herein to embrace any and all of the peptides, polypeptides and proteins of the present invention. Also forming part of the invention are polypeptides encoded by the polynucleotides of the invention, as well as fusion polypeptides comprising such polypeptides. The invention embodies HPPs from humans, including isolated or purified HPPs consisting of, consisting essentially of, or comprising an amino acid sequence selected from the group consisting of the sequences from Table 3. Further included are unmodified precursors, proteolytic precursors and intermediates of the sequence selected from the group consisting of the sequences from Table 3.

The present invention embodies an isolated, purified, and recombinant polypeptide fragment comprising a contiguous span of at least 3 amino acids, preferably at least 8 to 10 amino acids, of an amino acid sequence selected from the group consisting of the sequences from Table 3, wherein said fragment has an HPP biological activity. In an included embodiment, the contiguous stretch of amino acids comprises the site of a mutation or functional mutation, including a deletion, addition, swap or truncation of the amino acids in the HPP sequence. The invention also concerns the polypeptide encoded by the HPP nucleotide sequences of the invention, or a complementary sequence thereof or a

fragment thereof. Said polypeptide fragment may represent the actual peptide species that is present in human plasma. Said polypeptide fragment may be used, for example, to generate HPP-specific antibodies or to design another type of HPP-specific adsorbant.

One aspect of the invention pertains to isolated HPPs, and biologically active portions thereof, as well as polypeptide fragments suitable for use as immunogens to raise anti-HPP antibodies. In one embodiment, native HPP peptides can be isolated from plasma, cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, HPPs are produced by recombinant DNA techniques. Alternative to recombinant expression, an HPP can be synthesized chemically using peptide synthesis techniques, as described in the section titled "Chemical Manufacture of HPP compositions" and in Example 2.

Typically, biologically active portions comprise a domain or motif with at least one activity of an HPP. A biologically active HPP may, for example, comprise at least 1, 2, 3, or 5 amino acid changes from the sequence selected from the group consisting of the sequences from Table 3, or comprise at least 1%, 2%, 3%, 5%, 8%, 10% or 15% change in amino acids from the sequence selected from the group consisting of the sequences from Table 3.

Characterization of HPPs

The polypeptides of the invention, HPPs, are defined by the polypeptides of Table 3 and the accession numbers listed in Table 1. These peptides were isolated from human plasma and characterized according to the MicroProt® method, as described in Example 1.
For each HPP, Table 1 provides:

- an accession number in a public database, corresponding to the related polypeptide sequence;
- the amino acid positions defining the observed polypeptide with respect to the polypeptide in the public database.
- a classification into three categories, according to the following keys:
  - a: proteins not previously known to be plasmatic, most probably secreted.
  - b: proteins not previously known to be plasmatic, most probably from cellular leakage.
  - c: proteins not classified – most of them are new proteins, e.g. predicted from DNA.

Most of the accession numbers listed in Table 1 are references for the SwissPROT/TrEMBL databases, both of which are publicly available, for example at: http://www.expasy.ch. HPPs 40-57,

however, are defined as sequences appearing in published patent applications, as detailed in Table 1. Furthermore, the accession numbers for HPPs 58-61 correspond to predicted protein sequences obtained by running a number of softwares on GenBank entries, as detailed in Table 1. The accession numbers for HPPs 1-4 represent proteins entries available from NCBI, at http://www.ncbi.nlm.nih.gov/. Finally, the accession number for HPP 5 represents an EST, whose sequence is available from the dbEST database, for example from NCBI, at http://www.ncbi.nlm.nih.gov/

Table 1

Table 1			
Protein	**Accession Number**	**Amino Acids**	**Category**
HPP 1	AAH22362	1-239	c
HPP 2	AAH22823	1-233	c
HPP 3	AAH24178	1-643	c
HPP 4	AAH28090	1-234	c
HPP 5	N93909	aas 51-52 of translation in Frame 2	c
HPP 6	O00187	16-444	a
HPP 7	O00508	1-1587	a
HPP 8	O75368	1-114	b
HPP 9	O76076	1-250	a
HPP 10	O95135	1-1051	c
HPP 11	P00167	1-133	b
HPP 12	P00695	19-148	a
HPP 13	P01253	1-43	b
HPP 14	P02100	1-146	b
HPP 15	P02144	1-153	b
HPP 16	P04216	20-130	a
HPP 17	P05023	6-1023	b
HPP 18	P05060	21-677	a
HPP 19	P05092	1-164	b
HPP 20	P06703	1-90	b
HPP 21	P07108	1-86	b
HPP 22	P08493	20-96	a
HPP 23	P10645	272-319	a

Table 1

Protein	Accession Number	Amino Acids	Category
HPP 24	P11082	1-309	b
HPP 25	P12111	26-3176	a
HPP 26	P12273	29-146	a
HPP 27	P19957	23-117	a
HPP 28	P20071	1-107	b
HPP 29	P23142	30-703	a
HPP 30	P25490	1-414	b
HPP 31	P28799	18-593	a
HPP 32	P28799	281-336	a
HPP 33	P28827	21-1452	a
HPP 34	P32119	1-198	b
HPP 35	P39060	1334-1516	a
HPP 36	P48052	113-417	a
HPP 37	P52758	1-137	b
HPP 38	P58062	20-85	a
HPP 39	SEQ ID NO:158 from WO00/53753	1-99	c
HPP 40	Human hemoglobin adult beta protein (from US 6,172,039)	1-146	c
HPP 41	Mature human apolipoprotein E (apoE) isoprotein, apoE3 (from WO01/77136)	1-299	c
HPP 42	Human apo A-I protein (from WO02/40501)	1-243	c
HPP 43	SEQ ID NO: 2764 from EP1130094	1-493	c
HPP 44	Sequence of human apolipoprotein (from JP63237795)	1-77	c
HPP 45	Anti-rhesus D recombinant antibody D7C2 light chain (from FR2724182)	1-238	c
HPP 46	Human novel protein #335 (from WO01/55437)	1-384	c
HPP 47	Human PRO polypeptide sequence #234 (from WO01/68848)	1-97	c
HPP 48	Novel human secreted protein #3710 (from WO01/79449)	1-532	c
HPP 49	Mature protein sequence of antithrombin III (ATIII) (from WO98/36085)	1-432	c
HPP 50	SEQ ID 78 of WO99/16889.	1-127	c

Table 1			
Protein	**Accession Number**	**Amino Acids**	**Category**
HPP 51	AlphaE subunit of human fibrinogen (from WO00/09562)	1-847	c
HPP 52	SEQ ID No 32677 from WO01/75067	1-631	c
HPP 53	SEQ ID No 49662 from WO01/75067	1-250	c
HPP 54	SEQ ID No 59102 from WO01/75067	1-1196	c
HPP 55	genscan predicted polypeptide on NT_011687.5 at 1589772..1690791 - orientation: false	1-194	c
HPP 56	genscan predicted polypeptide on NT_008646.5 at 3027135..3076117 - orientation: true	1-141	c
HPP 57	genscan predicted polypeptide on NT_026966.2 at 269455..296792 - orientation: true	1-242	c
HPP 58	FGENESH predicted polypeptide on NT_026230.2 at 370496..630074 - orientation: true	1-1372	c
HPP 59	Q06141	27-175	a
HPP 60	Q13228	1-472	b
HPP 61	Q14212	21-1033	c
HPP 62	Q15828	29-149	a
HPP 63	Q16610	20-540	a
HPP 64	Q92520	1-227	a
HPP 65	Q96B73	1-370	b
HPP 66	Q96E61	1-236	c
HPP 67	Q96I69	1-233	c
HPP 68	Q96JD0	1-116	c
HPP 69	Q96JY4	1-811	c
HPP 70	Q96NZ9	1-151	a
HPP 71	Q9BRV0	1-500	c
HPP 72	Q9BSM9	1-170	c
HPP 73	Q9BTZ2	1-278	c
HPP 74	Q9HAL8	1-286	c
HPP 75	Q9NQ76	18-525	a
HPP 76	Q9NS71	1-199	b

Table 1			
Protein	**Accession Number**	**Amino Acids**	**Category**
HPP 77	Q9UK55	22-444	a
HPP 78	Q9UNN8	18-238	a
HPP 79	Q9UP60	1-384	c

The HPPs of the invention are all less than or around 20kD in molecular weight. Clear identification of low abundance proteins (leptin and ghrelin) and peptides (bradykinin) confirms the sensitivity of the detection methods of the invention.

The first separation is on a cation exchange chromatography column, which is eluted with increasing salt concentration. Eighteen fractions are collected. The CEX column in Table 3 lists which fraction contained tryptic peptides for each HPP. Table 2 provides the NaCl concentration at which each fraction was eluted, according to the protocol described in Step 3 of Example 1 herein. Separation by cation exchange provides an indication of the overall positive charge of a polypeptide species. Cation exchange is followed by a reverse phase HPLC separation. The RP1 column in Table 3 lists in which of the 30 fractions tryptic peptides eluted for each HPP. Table 2 provides the elution conditions (%B), according to the protocol described in Step 4 of Example 1. Separation by reverse phase provides an indication of the overall hydrophobicity of a polypeptide species. Finally, for each HPP, Table 3 provides for each CEX fraction and for each RP1 fraction, the list of tryptics detected in these fractions, along with the RP2 fractions (within parenthesis after each tryptic sequence) where these tryptics were detected.

Table 2

CEX Fraction Number	NaCl Concentration (mM)	RP1 Fraction Number	% B
1-5	75	1	4.1
6-8	100	2	12.5
9-14	175	3	20.8
15-16	225	4	25.96
17	275	5	27.88
18	1000	6	29.8
		7	31.73
		8	33.65
		9	35.7
		10	37.5
		11	39.42
		12	41.34
		13	43.27
		14	45.2
		15	47.1
		16	49.02
		17	50.95
		18	52.87
		19	54.8
		20	56.71
		21	58.64
		22	60.56
		23	62.48
		24	64.4
		25	68.25
		26	69
		27	70.17
		28	72.1
		29	74
		30	87.5

Table 3

Table 3			
Protein	**CEX**	**RP1**	**Tryptic Sequence (RP2 fractions)**
HPP 1	1	11	TVAAPSVFIFPPSDEQLK (24)
HPP 1	6	13	DSTYSLSSTLTLSK (13), FSGSGSGTDFTLK (13-15), RTVAAPSVFIFPPSDEQLK (14-15, 13), SGTASVVCLLNNFYPR (13-15), TVAAPSVFIFPPSDEQLK (13-14), VDNALQSGNSQESVTEQDSK (13-15), VYACEVTHQGLSSPVTK (13-15)
HPP 1	7	11	DSTYSLSSTLTLSK (19, 21), FSGSGSGTDFTLK (20), RTVAAPSVFIFPPSDEQLK (19-21), SGTASVVCLLNNFYPR (19-21), TVAAPSVFIFPPSDEQLK (19-21), VDNALQSGNSQESVTEQDSK (19-21), VYACEVTHQGLSSPVTK (19-21)
HPP 1	7	14	DSTYSLSSTLTLSK (8, 11), FSGSGSGTDFTLK (11), RTVAAPSVFIFPPSDEQLK (8), SGTASVVCLLNNFYPR (8, 11), TVAAPSVFIFPPSDEQLK (11), VDNALQSGNSQESVTEQDSK (8), VYACEVTHQGLSSPVTK (8, 11)
HPP 1	8	13	DSTYSLSSTLTLSK (11), FSGSGSGTDFTLK (11), RTVAAPSVFIFPPSDEQLK (11), SGTASVVCLLNNFYPR (11), VYACEVTHQGLSSPVTK (11)
HPP 1	8	14	FSGSGSGTDFTLK (13), SGTASVVCLLNNFYPR (13), TVAAPSVFIFPPSDEQLK (13), VDNALQSGNSQESVTEQDSK (13), VYACEVTHQGLSSPVTK (13)
HPP 1	8	15	HKVYACEVTHQGLSSPVTK (15), RTVAAPSVFIFPPSDEQLK (15), SGTASVVCLLNNFYPR (15), VYACEVTHQGLSSPVTK (15)
HPP 1	9	13	DSTYSLSSTLTLSK (13), FSGSGSGTDFTLK (13), RTVAAPSVFIFPPSDEQLK (13), SGTASVVCLLNNFYPR (13), VDNALQSGNSQESVTEQDSK (13), VYACEVTHQGLSSPVTK (13)
HPP 2	1	12	YAASSYLSLTPEQWK (20)
HPP 2	8	15	AAPSVTLFPPSSEELQANK (14), ITCSGDALPK (14), LTVLGQPK (14), SYSCQVTHEGSTVEK (14), YAASSYLSLTPEQWK (14)
HPP 3	2	8	FSEAITVLLSWIER (10)
HPP 3	2	13	FSEAITVLLSWIER (17)
HPP 3	2	14	FSEAITVLLSWIER (21)
HPP 3	2	15	FSEAITVLLSWIER (16)
HPP 3	3	17	FSEAITVLLSWIER (9-10)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 3	3	19	FSEAITVLLSWIER (9)
HPP 3	5	24	FSEAITVLLSWIER (3)
HPP 3	6	17	FSEAITVLLSWIER (10)
HPP 4	8	14	FSGSNSGNTATLTISR (7), LTVLGQPK (7), YAASSYLSLTPEQWK (7)
HPP 5	1	5	CDSFSASIL (12)
HPP 5	1	7	CDSFSASIL (7)
HPP 6	13	15	AGYVLHR (9), LASPGFPGEYANDQER (9)
HPP 6	13	16	LYFTHFDLELSHLCEYDFVK (7)
HPP 6	13	18	WPEPVFGR (6)
HPP 6	13	19	LASPGFPGEYANDQER (6)
HPP 6	13	20	WPEPVFGR (5)
HPP 6	13	22	WPEPVFGR (4)
HPP 6	13	23	LYFTHFDLELSHLCEYDFVK (3), WPEPVFGR (3)
HPP 6	14	14	AGYVLHR (8), APGKDTFYSLGSSLDITFR (8), LASPGFPGEYANDQER (9), LYFTHFDLELSHLCEYDFVK (8-9), VLATLCGQESTDTER (9), WPEPVFGR (9), WTLTAPPGYR (8-9, 11)
HPP 6	14	15	LASPGFPGEYANDQER (9, 11), LASPGFPGEYANDQERR (9), LYFTHFDLELSHLCEYDFVK (11), VLATLCGQESTDTER (9), WPEPVFGR (9, 11), WTLTAPPGYR (9, 11)
HPP 6	14	16	AGYVLHR (7-8), DTFYSLGSSLDITFR (7-12), LASPGFPGEYANDQER (7-12), LYFTHFDLELSHLCEYDFVK (7-18, 21, 22), TPLGPKWPEPVFGR (7-8), VLATLCGQESTDTER (7-8, 10, 11, 12), WPEPVFGR (7-8, 10, 12), WTLTAPPGYR (7, 11, 12)
HPP 6	14	17	AGYVLHR (12-14), DTFYSLGSSLDITFR (7-8), LASPGFPGEYANDQER (7-9, 14, 15), LASPGFPGEYANDQERR (13), LYFTHFDLELSHLCEYDFVK (7-8), TPLGPKWPEPVFGR (16), WPEPVFGR (7-9, 14, 15, 17, 19, 23), WTLTAPPGYR (7-11, 13, 15, 17)
HPP 6	14	18	AGYVLHR (6-9), APGKDTFYSLGSSLDITFR (6), LASPGFPGEYANDQER (7-8), LYFTHFDLELSHLCEYDFVK (6-7), TPLGPKWPEPVFGR (6), VLATLCGQESTDTER (6), WPEPVFGR (6-7, 9, 10, 11, 14), WTLTAPPGYR (7-8)
HPP 6	14	19	AGYVLHR (6-10), APGKDTFYSLGSSLDITFR (6), DTFYSLGSSLDITFR (6), LASPGFPGEYANDQER (6-7, 9), LASPGFPGEYANDQERR (8), LYFTHFDLELSHLCEYDFVK (6-7), TPLGPKWPEPVFGR (7-8), VLATLCGQESTDTER (6-7), WPEPVFGR (6-12), WTLTAPPGYR (6-7, 11)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 6	14	20	AGYVLHR (6-8), APGKDTFYSLGSSLDITFR (5), DTFYSLGSSLDITFR (6), LASPGFPGEYANDQER (6-7), LYFTHFDLELSHLCEYDFVK (5), RWTLTAPPGYR (5), TPLGPKWPEPVFGR (4-5), VLATLCGQESTDTER (10), WPEPVFGR (6-7, 10, 17), WTLTAPPGYR (5, 8)
HPP 6	14	21	AGYVLHR (6-7), DTFYSLGSSLDITFR (5-7), LASPGFPGEYANDQER (5, 7, 9, 10, 12, 15, 16, 17), LASPGFPGEYANDQERR (4), LYFTHFDLELSHLCEYDFVK (5-7, 9, 11, 12, 14), VLATLCGQESTDTER (5-7, 10), WPEPVFGR (5-6, 9, 14), WTLTAPPGYR (5-6, 8)
HPP 6	14	22	AGYVLHR (4, 6, 7), APGKDTFYSLGSSLDITFR (3), DTFYSLGSSLDITFR (5), LASPGFPGEYANDQER (3, 11, 12, 13), LYFTHFDLELSHLCEYDFVK (3-4), VLATLCGQESTDTER (3), WPEPVFGR (3-9, 11, 14), WTLTAPPGYR (3-9, 13)
HPP 6	14	23	AGYVLHR (3-9, 11, 12), DTFYSLGSSLDITFR (4, 7), LASPGFPGEYANDQER (3-6, 8), LASPGFPGEYANDQERR (3), LYFTHFDLELSHLCEYDFVK (3-7, 11, 12), TPLGPKWPEPVFGR (3, 5), VLATLCGQESTDTER (3-4, 10), WPEPVFGR (3-6, 8, 9, 10, 13, 16), WTLTAPPGYR (3, 5, 7, 11, 12)
HPP 6	14	24	AGYVLHR (3-5), DTFYSLGSSLDITFR (2-3), LASPGFPGEYANDQER (1-8, 12), LYFTHFDLELSHLCEYDFVK (1-5, 7, 8, 9), VLATLCGQESTDTER (1-6), WPEPVFGR (1-6, 8, 9, 13), WTLTAPPGYR (1-4, 6, 8, 11, 12)
HPP 6	14	25	AGYVLHR (2-3, 5), DTFYSLGSSLDITFR (2-5), LASPGFPGEYANDQER (1, 5, 6, 7, 8), LYFTHFDLELSHLCEYDFVK (2-9, 11), VLATLCGQESTDTER (1-6, 8), WPEPVFGR (2-3, 5, 6, 7, 8, 9, 10), WTLTAPPGYR (1-5, 7, 8, 9)
HPP 6	14	26	AGYVLHR (1), DTFYSLGSSLDITFR (8), LASPGFPGEYANDQER (1-2, 7), LYFTHFDLELSHLCEYDFVK (5, 8), VLATLCGQESTDTER (3, 5, 7, 9), WPEPVFGR (1, 4, 7), WTLTAPPGYR (1-5, 8)
HPP 6	14	27	AGYVLHR (6), DTFYSLGSSLDITFR (1-2), LASPGFPGEYANDQER (1-2, 10), LYFTHFDLELSHLCEYDFVK (1, 4, 7, 8), TPLGPKWPEPVFGR (9), VLATLCGQESTDTER (1, 3, 10), WPEPVFGR (1-2, 4, 5, 7, 8), WTLTAPPGYR (1, 3, 5, 7)
HPP 6	14	28	AGYVLHR (3, 5, 6, 8), DTFYSLGSSLDITFR (3), LASPGFPGEYANDQER (4-7, 10), LYFTHFDLELSHLCEYDFVK (3-6), VLATLCGQESTDTER (2-4, 6, 10), WPEPVFGR (3-6, 8), WTLTAPPGYR (2-3, 6, 8)
HPP 6	14	29	AGYVLHR (3), DTFYSLGSSLDITFR (3), LASPGFPGEYANDQER (3-4, 8, 9, 10), LYFTHFDLELSHLCEYDFVK (3-4, 6, 7, 9), VLATLCGQESTDTER (3-4), WPEPVFGR (6, 9, 11, 12), WTLTAPPGYR (3-5, 7, 9, 10, 11)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 6	14	30	AGYVLHR (3), DTFYSLGSSLDITFR (3), LASPGFPGEYANDQER (3-8, 12), LYFTHFDLELSHLCEYDFVK (3-4), VLATLCGQESTDTER (3-8), WPEPVFGR (3), WTLTAPPGYR (3-5, 7)
HPP 6	17	22	WPEPVFGR (3)
HPP 7	10	10	VPEGFTCR (8)
HPP 7	12	9	MACVDINECDEAEAASPLCVNAR (10), VPEGFTCR (8-9, 11)
HPP 7	12	10	VPEGFTCR (10-11)
HPP 7	12	13	VPEGFTCR (11)
HPP 8	7	10	GDYDAFFEAR (15), QQDVLGFLEANK (14), VYIASSSGSTAIK (13)
HPP 8	7	11	ENNAVYAFLGLTAPPGSK (15), GDYDAFFEAR (14-15), QQDVLGFLEANK (15), VYIASSSGSTAIK (14-15)
HPP 8	7	12	GDYDAFFEAR (8-10), KQQDVLGFLEANK (9), VYIASSSGSTAIK (8-9)
HPP 8	7	13	VYIASSSGSTAIK (9)
HPP 9	6	9	CPLGVPLVLDGCGCCR (17)
HPP 9	7	10	GALCLLAEDDSSCEVNGR (12)
HPP 10	2	21	IAMENDDGR (7, 10)
HPP 10	2	22	IAMENDDGR (6)
HPP 11	12	10	YYTLEEIQK (9)
HPP 11	12	11	FLEEHPGGEEVLR (11), YYTLEEIQK (10-11)
HPP 12	2	14	STDYGIFQINSR (6)
HPP 12	15	2	AWVAWR (1), LGMDGYR (1), STDYGIFQINSR (1), WESGYNTR (1)
HPP 12	17	13	TPGAVNACHLSCSALLQDNIADAVACAK (9)
HPP 13	7	3	NPLPSKETIEQEK (14)
HPP 13	7	4	NPLPSKETIEQEK (8), SDKPDMAEIEK (8, 11), SDKPDMAEIEKFDK (7-8, 11), TETQEKNPLPSK (7-8, 11)
HPP 13	7	8	SDKPDMAEIEKFDK (5)
HPP 13	8	5	NPLPSKETIEQEK (12), SDKPDMAEIEKFDK (13), TETQEKNPLPSK (13)
HPP 14	14	15	LLVVYPWTQR (16), LSELHCDK (16)
HPP 14	14	19	LLVVYPWTQR (8, 10), LSELHCDK (8), LVSAVAIALAHKYH (10)
HPP 15	17	15	HGATVLTALGGILK (11)
HPP 15	17	18	HGATVLTALGGILK (6)
HPP 15	17	28	YLEFISECIIQVLQSK (3)
HPP 15	18	16	HGATVLTALGGILK (7)
HPP 15	18	17	HGATVLTALGGILK (8)
HPP 15	18	18	VEADIPGHGQEVLIR (6)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 15	18	26	HGATVLTALGGILK (3)
HPP 16	5	9	VTSLTACLVDQSLR (15)
HPP 16	6	9	TNFTSKYNMK (13), VLYLSAFTSK (12-13), VTSLTACLVDQSLR (12-13)
HPP 16	6	10	VTSLTACLVDQSLR (8)
HPP 16	7	8	VTSLTACLVDQSLR (13)
HPP 17	11	18	RAVAGDASESALLK (6)
HPP 17	11	24	RAVAGDASESALLK (2)
HPP 17	13	21	RAVAGDASESALLK (5)
HPP 18	12	11	CIIEVLSNALSK (8)
HPP 18	13	11	CIIEVLSNALSK (8)
HPP 19	13	14	VSFELFADK (8)
HPP 19	13	15	FEDENFILK (9), KITIADCGQLE (8)
HPP 19	14	13	FEDENFILK (10), KITIADCGQLE (9)
HPP 19	14	14	FEDENFILK (8), VSFELFADK (8)
HPP 19	14	15	EGMNIVEAMER (9-10), FEDENFILK (8-10), HTGPGILSMANAGPNTNGSQFFICTAK (9), VNPTVFFDIAVDGEPLGR (9)
HPP 20	17	21	LQDAEIAR (10)
HPP 20	18	21	LMEDLDR (11)
HPP 20	18	22	DQEVNFQEYVTFLGALALIYNEALK (7), NKDQEVNFQEYVTFLGALALIYNEALK (7)
HPP 21	13	10	QATVGDINTERPGMLDFTGK (9)
HPP 21	13	11	AYINKVEELK (14)
HPP 21	13	12	QATVGDINTERPGMLDFTGK (9), TKPSDEEMLFIYGHYK (9), WDAWNELK (9)
HPP 21	14	11	TKPSDEEMLFIYGHYK (11)
HPP 22	5	7	NANTFISPQQR (11-12)
HPP 22	6	6	NANTFISPQQR (8)
HPP 22	8	8	NANTFISPQQR (7)
HPP 22	10	7	NANTFISPQQR (7-8, 11), YESHESMESYELNPFINRR (12)
HPP 22	10	8	NANTFISPQQR (6)
HPP 22	11	8	NANTFISPQQR (8-9, 11, 12)
HPP 22	11	11	NANTFISPQQR (8)
HPP 22	12	8	NANTFISPQQR (6-7, 12)
HPP 22	12	9	NANTFISPQQR (7-9)
HPP 22	13	8	NANTFISPQQR (8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 22	13	9	NANTFISPQQR (8-12)
HPP 22	14	6	NANTFISPQQR (10)
HPP 22	14	7	NANTFISPQQR (10-14)
HPP 22	14	9	NANTFISPQQR (8)
HPP 22	14	11	NANTFISPQQR (7)
HPP 22	15	7	NANTFISPQQR (16)
HPP 22	16	8	NANTFISPQQR (7)
HPP 23	2	8	SEALAVDGAGKPGAEEAQDPEGK (9)
HPP 23	3	9	SEALAVDGAGKPGAEEAQDPEGK (9)
HPP 24	15	11	QLNENQVR (17)
HPP 24	17	14	QLNENQVR (7-8)
HPP 24	17	21	QLNENQVR (4)
HPP 24	17	28	QLNENQVR (1)
HPP 24	17	30	QLNENQVR (2)
HPP 25	10	9	FWYGGCGGNENK (14, 16), VCAPVLAKPGVISVMGT (17)
HPP 25	10	10	VCAPVLAKPGVISVMGT (11)
HPP 25	11	8	FWYGGCGGNENK (13-14), VCAPVLAKPGVISVMGT (15), WYYDPNTK (13)
HPP 25	11	9	DEGTCRDFILK (13), FWYGGCGGNENK (12-17), VCAPVLAKPGVISVMGT (13, 15, 16, 17, 18), WYYDPNTK (14, 16, 17)
HPP 25	11	10	DFILK (10), FWYGGCGGNENK (9-10), VCAPVLAKPGVISVMGT (9-10, 14)
HPP 25	11	11	FWYGGCGGNENK (8-10), WYYDPNTK (9)
HPP 25	11	12	FWYGGCGGNENK (7), VCAPVLAKPGVISVMGT (7)
HPP 25	11	13	FWYGGCGGNENK (7), VCAPVLAKPGVISVMGT (7)
HPP 25	12	9	FWYGGCGGNENK (9-12), VCAPVLAKPGVISVMGT (9-12), WYYDPNTK (9-12)
HPP 25	12	10	FWYGGCGGNENK (8-10), VCAPVLAKPGVISVMGT (8-10), WYYDPNTK (8)
HPP 26	4	17	YTACLCDDNPK (12)
HPP 26	5	20	ELGICPDDAAVIPIKNNR (6)
HPP 26	5	21	FYTIEILKVE (7), TYLISSIPLQGAFNYK (7), YTACLCDDNPK (7)
HPP 26	5	25	ELGICPDDAAVIPIK (4)
HPP 26	15	2	FYTIEILKVE (1)
HPP 27	5	8	AQEPVKGPVSTKPGSCPIILIR (7-8), VPFNGQDPVK (7)
HPP 27	6	6	VPFNGQDPVK (10)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 27	6	8	AQEPVKGPVSTKPGSCPIILIR (7-8), CAMLNPPNR (7-8), CLKDTDCPGIK (7), VPFNGQDPVK (7), VPFNGQDPVKGQVSVK (7)
HPP 27	8	8	AQEPVKGPVSTKPGSCPIILIR (7), CAMLNPPNR (7)
HPP 27	9	8	VPFNGQDPVK (7)
HPP 27	10	8	GPVSTKPGSCPIILIR (8)
HPP 28	10	11	GVQVETISPGDGR (12)
HPP 28	10	12	GVQVETISPGDGR (9)
HPP 28	11	11	GVQVETISPGDGR (11)
HPP 28	12	12	GVQVETISPGDGR (8)
HPP 28	12	13	GVQVETISPGDGR (12)
HPP 29	13	12	DVLLEACCADGHR (6)
HPP 29	13	13	AAQAQGQSCEYSLMVGYQCGQVFR (7)
HPP 30	3	21	MFRDNSAMR (6)
HPP 30	4	14	MFRDNSAMR (13)
HPP 30	4	23	MFRDNSAMR (5, 7)
HPP 30	6	23	MFRDNSAMR (4)
HPP 31	5	7	VHCCPHGAFCDLVHTR (13)
HPP 31	5	8	VHCCPHGAFCDLVHTR (11)
HPP 31	6	8	VHCCPHGAFCDLVHTR (8)
HPP 31	6	9	VHCCPHGAFCDLVHTR (8-9)
HPP 31	6	10	VHCCPHGAFCDLVHTR (7)
HPP 31	7	8	VHCCPHGAFCDLVHTR (8)
HPP 31	7	9	VHCCPHGAFCDLVHTR (8)
HPP 31	7	10	CDMEVSCPDGYTCCR (7), VHCCPHGAFCDLVHTR (7)
HPP 31	10	23	ARSCEK (12)
HPP 31	11	8	CITPTGTHPLAK (11)
HPP 32	7	5	DVKCDMEVSCPDGYTCCR (19-21)
HPP 32	7	6	CDMEVSCPDGYTCCR (11), DVKCDMEVSCPDGYTCCR (12)
HPP 32	7	7	CDMEVSCPDGYTCCR (11), DVKCDMEVSCPDGYTCCR (11-12)
HPP 32	7	8	CDMEVSCPDGYTCCR (7-8), DVKCDMEVSCPDGYTCCR (7-8)
HPP 32	7	10	CDMEVSCPDGYTCCR (7), DVKCDMEVSCPDGYTCCR (6)
HPP 32	8	7	CDMEVSCPDGYTCCR (11-13), DVKCDMEVSCPDGYTCCR (11-13)
HPP 32	8	8	CDMEVSCPDGYTCCR (8)
HPP 33	1	9	TYNGYWNTPLLPYK (24)
HPP 33	1	12	ANGETKIDCVQVATK (10), IDCVQVATK (11), IYFQAASR (8-9, 11)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 34	9	17	ATAVVDGAFK (15), EGGLGPLNIPLLADVTR (15-16), KEGGLGPLNIPLLADVTR (15-16), LGCEVLGVSVDSQFTHLAWINTPR (15), TDEGIAYR (15-16)
HPP 34	9	19	EGGLGPLNIPLLADVTR (8), KEGGLGPLNIPLLADVTR (8), QITVNDLPVGR (8)
HPP 34	9	20	KEGGLGPLNIPLLADVTR (7)
HPP 34	9	21	KEGGLGPLNIPLLADVTR (7)
HPP 34	10	19	EGGLGPLNIPLLADVTR (9), KEGGLGPLNIPLLADVTR (9), LGCEVLGVSVDSQFTHLAWINTPR (9), QITVNDLPVGR (9)
HPP 34	10	22	KEGGLGPLNIPLLADVTR (6)
HPP 34	10	23	KEGGLGPLNIPLLADVTR (6)
HPP 34	11	18	EGGLGPLNIPLLADVTR (9), KEGGLGPLNIPLLADVTR (10), QITVNDLPVGR (9)
HPP 34	11	19	KEGGLGPLNIPLLADVTR (11), LGCEVLGVSVDSQFTHLAWINTPR (11), QITVNDLPVGR (11)
HPP 34	11	21	KEGGLGPLNIPLLADVTR (8)
HPP 34	13	18	EGGLGPLNIPLLADVTR (9), KEGGLGPLNIPLLADVTR (9-10)
HPP 34	13	20	EGGLGPLNIPLLADVTR (8)
HPP 34	14	17	EGGLGPLNIPLLADVTR (18), KEGGLGPLNIPLLADVTR (18), LSEDYGVLK (18)
HPP 34	14	18	KEGGLGPLNIPLLADVTR (10)
HPP 34	14	21	EGGLGPLNIPLLADVTR (8)
HPP 34	14	22	KEGGLGPLNIPLLADVTR (7)
HPP 34	14	24	EGGLGPLNIPLLADVTR (5), KEGGLGPLNIPLLADVTR (5)
HPP 34	14	27	KEGGLGPLNIPLLADVTR (5)
HPP 34	14	28	KEGGLGPLNIPLLADVTR (6)
HPP 35	10	18	LQDLYSIVR (7)
HPP 35	11	17	DFQPVLHLVALNSPLSGGMR (9)
HPP 35	11	18	DFQPVLHLVALNSPLSGGMR (7)
HPP 35	15	18	DFQPVLHLVALNSPLSGGMR (7), TEAPSATGQASSLLGGR (7)
HPP 36	2	19	EWVTQATALWTANKIVSDYGK (11)
HPP 36	2	22	EWVTQATALWTANKIVSDYGK (8)
HPP 37	1	20	APGAIGPYSQAVLVDR (12), TTVLLADINDFNTVNEIYK (12)
HPP 37	1	24	TTVLLADINDFNTVNEIYK (6)
HPP 38	8	11	VQFLHDGSC (7-8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 39	9	16	ADEFLNWHALFESIK (9)
HPP 39	10	16	ADEFLNWHALFESIK (9), LPFLNWDAFPK (9)
HPP 39	11	15	ADEFLNWHALFESIK (14-17), ADEFLNWHALFESIKR (14), KLPFLNWDAFPK (14, 16, 17), LPFLNWDAFPK (14)
HPP 39	11	16	ADEFLNWHALFESIK (9-10, 12)
HPP 39	12	16	ADEFLNWHALFESIK (9), KLPFLNWDAFPK (9)
HPP 40	5	23	EFTPPVQAAYQK (5)
HPP 40	6	13	EFTPPVQAAYQK (9), VVAGVANALAHK (9)
HPP 40	9	16	EFTPPVQAAYQK (12), FFESFGDLSTPDAVMGNPK (12-14, 16), VNVDEVGGEALGR (12-14, 16)
HPP 40	9	19	EFTPPVQAAYQK (7), FFESFGDLSTPDAVMGNPK (8), VLGAFSDGLAHLDNLK (8)
HPP 40	10	16	LLVVYPWTQR (9)
HPP 40	10	17	EFTPPVQAAYQK (11), FFESFGDLSTPDAVMGNPK (11-13), GTFATLSELHCDK (12), KVLGAFSDGLAHLDNLK (10-13), LLGNVLVCVLAHHFGK (12), LLVVYPWTQR (10-11), SAVTALWGK (12), VLGAFSDGLAHLDNLK (11-13), VNVDEVGGEALGR (12-13), VVAGVANALAHK (11)
HPP 40	10	18	EFTPPVQAAYQK (7-10), FFESFGDLSTPDAVMGNPK (8-10), KVLGAFSDGLAHLDNLK (8), LLGNVLVCVLAHHFGK (8), LLVVYPWTQR (7, 9, 10), VLGAFSDGLAHLDNLK (9), VNVDEVGGEALGR (10), VVAGVANALAHK (7-8)
HPP 40	11	15	VVAGVANALAHK (14)
HPP 40	11	16	EFTPPVQAAYQK (12), FFESFGDLSTPDAVMGNPK (11-13), GTFATLSELHCDK (11), LHVDPENFR (11-12), LLGNVLVCVLAHHFGK (11-13), LLVVYPWTQR (9-13), SAVTALWGK (12), VLGAFSDGLAHLDNLK (12-13), VNVDEVGGEALGR (12-13), VVAGVANALAHK (10-13)
HPP 40	11	17	EFTPPVQAAYQK (11-14, 16, 17), FFESFGDLSTPDAVMGNPK (12-16), GTFATLSELHCDK (12, 14), GTFATLSELHCDKLHVDPENFR (13, 15), KVLGAFSDGLAHLDNLK (12-16), LHVDPENFR (11-12), LLGNVLVCVLAHHFGK (11-17), LLVVYPWTQR (11-16), SAVTALWGK (12-15), VHLTPEEK (11, 13, 14, 15, 16), VLGAFSDGLAHLDNLK (12-14, 16), VNVDEVGGEALGR (11-16), VVAGVANALAHK (11-15), VVAGVANALAHKYH (13)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 40	11	18	EFTPPVQAAYQK (8), FFESFGDLSTPDAVMGNPK (8-10), GTFATLSELHCDK (8), LHVDPENFR (8), LLVVYPWTQR (8, 10, 11, 12), SAVTALWGK (9), VLGAFSDGLAHLDNLK (8-11), VNVDEVGGEALGR (9), VVAGVANALAHK (9)
HPP 40	11	19	EFTPPVQAAYQK (8-9), FFESFGDLSTPDAVMGNPK (8-9), LHVDPENFR (8), LLVVYPWTQR (8-9), SAVTALWGK (8), VNVDEVGGEALGR (8)
HPP 40	11	20	EFTPPVQAAYQK (7), FFESFGDLSTPDAVMGNPK (7-8), GTFATLSELHCDK (7-8), LLVVYPWTQR (7-8), VLGAFSDGLAHLDNLK (7-8), VNVDEVGGEALGR (7), VVAGVANALAHK (7)
HPP 40	11	21	FFESFGDLSTPDAVMGNPK (8), KVLGAFSDGLAHLDNLK (7), LLGNVLVCVLAHHFGK (7), LLVVYPWTQR (8-9), VLGAFSDGLAHLDNLK (7), VNVDEVGGEALGR (7)
HPP 40	11	22	LLVVYPWTQR (7)
HPP 40	12	16	FFESFGDLSTPDAVMGNPK (10), LLGNVLVCVLAHHFGK (10), LLVVYPWTQR (10-11), VNVDEVGGEALGR (10-11), VVAGVANALAHK (10)
HPP 40	12	17	EFTPPVQAAYQK (7, 9), FFESFGDLSTPDAVMGNPK (7-8), GTFATLSELHCDKLHVDPENFR (8), KVLGAFSDGLAHLDNLK (7), LHVDPENFR (9), VLGAFSDGLAHLDNLK (7, 9), VNVDEVGGEALGR (7, 9), VVAGVANALAHK (8-9), VVAGVANALAHKYH (8)
HPP 40	12	18	EFTPPVQAAYQK (7-8), FFESFGDLSTPDAVMGNPK (7-8), GTFATLSELHCDK (7-8), KVLGAFSDGLAHLDNLK (6, 8), LLGNVLVCVLAHHFGK (7), LLVVYPWTQR (7), SAVTALWGK (7-8), VHLTPEEK (7), VLGAFSDGLAHLDNLK (7-9), VNVDEVGGEALGR (6-9), VVAGVANALAHK (7-9)
HPP 40	12	19	FFESFGDLSTPDAVMGNPK (8), GTFATLSELHCDK (8), KVLGAFSDGLAHLDNLK (8)
HPP 40	12	20	EFTPPVQAAYQK (6), LLGNVLVCVLAHHFGK (7), LLVVYPWTQR (6, 8), VLGAFSDGLAHLDNLK (6)
HPP 40	12	22	FFESFGDLSTPDAVMGNPK (5), VLGAFSDGLAHLDNLK (5), VNVDEVGGEALGR (5)
HPP 40	12	23	FFESFGDLSTPDAVMGNPK (5), LLVVYPWTQR (5), VHLTPEEK (5)
HPP 40	13	16	EFTPPVQAAYQK (10), FFESFGDLSTPDAVMGNPK (10), GTFATLSELHCDKLHVDPENFR (10), KVLGAFSDGLAHLDNLK (10), LLGNVLVCVLAHHFGK (10), LLVVYPWTQR (10), SAVTALWGK (10), VLGAFSDGLAHLDNLK (9-10)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 40	13	17	EFTPPVQAAYQK (12, 14), FFESFGDLSTPDAVMGNPK (10-11, 13, 14), KVLGAFSDGLAHLDNLK (12), LLGNVLVCVLAHHFGK (10, 12), LLVVYPWTQR (10-13), SAVTALWGK (11, 13, 14), VHLTPEEK (12, 14), VLGAFSDGLAHLDNLK (11-12), VNVDEVGGEALGR (10-15), VVAGVANALAHK (11-12)
HPP 40	13	18	EFTPPVQAAYQK (7-8), FFESFGDLSTPDAVMGNPK (8-9), GTFATLSELHCDK (8), KVLGAFSDGLAHLDNLK (7), LHVDPENFR (9), LLGNVLVCVLAHHFGK (7-8), LLVVYPWTQR (7-10), SAVTALWGK (8, 10), VHLTPEEK (7), VLGAFSDGLAHLDNLK (7-8), VNVDEVGGEALGR (7-8), VVAGVANALAHK (8-10)
HPP 40	13	19	EFTPPVQAAYQK (9, 11, 12), FFESFGDLSTPDAVMGNPK (8-12), GTFATLSELHCDK (9, 12), LHVDPENFR (9, 12), LLGNVLVCVLAHHFGK (9-10), LLVVYPWTQR (8-11), SAVTALWGK (12), VHLTPEEK (12), VLGAFSDGLAHLDNLK (8, 10, 11), VNVDEVGGEALGR (7, 9, 11, 12), VVAGVANALAHK (9, 11)
HPP 40	13	20	FFESFGDLSTPDAVMGNPK (7-8), LLVVYPWTQR (9-10), VLGAFSDGLAHLDNLK (7-8)
HPP 40	13	21	EFTPPVQAAYQK (7), LLVVYPWTQR (7-8)
HPP 40	13	22	FFESFGDLSTPDAVMGNPK (6), LLGNVLVCVLAHHFGK (5), LLVVYPWTQR (5), VLGAFSDGLAHLDNLK (5-6), VNVDEVGGEALGR (5-6), VVAGVANALAHK (5)
HPP 40	13	23	LLVVYPWTQR (6), VNVDEVGGEALGR (5), VVAGVANALAHK (5)
HPP 40	13	24	FFESFGDLSTPDAVMGNPK (4), LLVVYPWTQR (4), SAVTALWGK (4), VHLTPEEK (4), VVAGVANALAHK (4)
HPP 40	14	14	EFTPPVQAAYQK (12), FFESFGDLSTPDAVMGNPK (9-10), KVLGAFSDGLAHLDNLK (10), LLVVYPWTQR (10), VLGAFSDGLAHLDNLK (11), VNVDEVGGEALGR (9-10), VVAGVANALAHK (11)
HPP 40	14	15	EFTPPVQAAYQK (14, 16, 17, 18, 19), FFESFGDLSTPDAVMGNPK (10, 15, 16, 17, 18, 19), GTFATLSELHCDK (15-18), KVLGAFSDGLAHLDNLK (16, 18), LLGNVLVCVLAHHFGK (15-18), LLGNVLVCVLAHHFGKEFTPPVQAAYQK (16), LLVVYPWTQR (15-17), SAVTALWGK (15-17), SAVTALWGKVNVDEVGGEALGR (16-17), VHLTPEEK (16-17), VLGAFSDGLAHLDNLK (15-17), VNVDEVGGEALGR (9-10, 16, 17), VVAGVANALAHK (14-15, 17, 18, 19)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 40	14	16	EFTPPVQAAYQK (11-13, 16), FFESFGDLSTPDAVMGNPK (11-16), GTFATLSELHCDK (11-12, 14), GTFATLSELHCDKLHVDPENFR (13), KVLGAFSDGLAHLDNLK (11-12, 14, 15), LHVDPENFR (11-12, 15), LLGNVLVCVLAHHFGK (9-14), LLVVYPWTQR (8-15), SAVTALWGK (11-13, 15), VHLTPEEK (11, 13), VLGAFSDGLAHLDNLK (8, 11, 12, 13, 14, 15), VNVDEVGGEALGR (10-16), VVAGVANALAHK (10-11, 14, 15)
HPP 40	14	17	EFTPPVQAAYQK (9-10, 12, 13, 14, 15), FFESFGDLSTPDAVMGNPK (11-15), GTFATLSELHCDK (10-14), KVLGAFSDGLAHLDNLK (9, 12, 13, 14), LHVDPENFR (12-14), LLGNVLVCVLAHHFGK (9-10, 12, 14, 16), LLVVYPWTQR (8, 11, 12, 13, 14, 15, 16), SAVTALWGK (11-14), VHLTPEEK (11-14), VLGAFSDGLAHLDNLK (9-10, 12, 13, 14, 15), VNVDEVGGEALGR (9-15), VVAGVANALAHK (9-10, 12, 13, 15)
HPP 40	14	18	EFTPPVQAAYQK (8-9), FFESFGDLSTPDAVMGNPK (8-11), GTFATLSELHCDK (8, 10), KVLGAFSDGLAHLDNLK (8, 10), LLGNVLVCVLAHHFGK (7-10), LLVVYPWTQR (9), SAVTALWGK (8), VHLTPEEK (8), VLGAFSDGLAHLDNLK (7-10), VNVDEVGGEALGR (7-9), VVAGVANALAHK (7-9)
HPP 40	14	19	EFTPPVQAAYQK (7-11), FFESFGDLSTPDAVMGNPK (7-14), GTFATLSELHCDK (8-12), GTFATLSELHCDKLHVDPENFR (8), KVLGAFSDGLAHLDNLK (7-8, 10, 12), LHVDPENFR (8-10), LLGNVLVCVLAHHFGK (7-12), LLGNVLVCVLAHHFGKEFTPPVQAAYQK (8), LLVVYPWTQR (8-10, 12), SAVTALWGK (8-10), VHLTPEEK (7-12), VLGAFSDGLAHLDNLK (7-12), VNVDEVGGEALGR (8-13), VVAGVANALAHK (8-11), VVAGVANALAHKYH (8)
HPP 40	14	20	EFTPPVQAAYQK (7), FFESFGDLSTPDAVMGNPK (7-9), GTFATLSELHCDK (7-8), GTFATLSELHCDKLHVDPENFR (6), KVLGAFSDGLAHLDNLK (7), LHVDPENFR (7), LLGNVLVCVLAHHFGK (6), LLVVYPWTQR (6-7, 9, 10), SAVTALWGK (6-8), VHLTPEEK (6-7), VLGAFSDGLAHLDNLK (7-8), VNVDEVGGEALGR (6-8), VVAGVANALAHK (6-8)
HPP 40	14	21	EFTPPVQAAYQK (7-8), FFESFGDLSTPDAVMGNPK (6-8), GTFATLSELHCDK (7-8), KVLGAFSDGLAHLDNLK (6-7), LHVDPENFR (7-8), LLGNVLVCVLAHHFGK (6-8), LLVVYPWTQR (6-9), SAVTALWGK (6-8), VLGAFSDGLAHLDNLK (6-7), VNVDEVGGEALGR (6-9), VVAGVANALAHK (6-8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 40	14	22	EFTPPVQAAYQK (6), FFESFGDLSTPDAVMGNPK (5-6), GTFATLSELHCDK (5-6), KVLGAFSDGLAHLDNLK (6), LHVDPENFR (6), LLGNVLVCVLAHHFGK (5-6), LLVVYPWTQR (5-6), SAVTALWGK (5-6), VHLTPEEK (5-6), VLGAFSDGLAHLDNLK (6), VNVDEVGGEALGR (5-6), VVAGVANALAHK (5-6)
HPP 40	14	23	EFTPPVQAAYQK (5-6), FFESFGDLSTPDAVMGNPK (5-6), GTFATLSELHCDK (6), LLGNVLVCVLAHHFGK (5-6), LLVVYPWTQR (5-6), SAVTALWGK (5-6), SAVTALWGKVNVDEVGGEALGR (5), VHLTPEEK (5-6), VHLTPEEKSAVTALWGK (5), VLGAFSDGLAHLDNLK (5-6), VNVDEVGGEALGR (5-6), VVAGVANALAHK (5-6), VVAGVANALAHKYH (5)
HPP 40	14	24	EFTPPVQAAYQK (4), FFESFGDLSTPDAVMGNPK (4), GTFATLSELHCDK (3-4), KVLGAFSDGLAHLDNLK (4), LHVDPENFR (4), LLGNVLVCVLAHHFGK (3-5), LLGNVLVCVLAHHFGKEFTPPVQAAYQK (4), LLVVYPWTQR (4-5), SAVTALWGK (4), VHLTPEEK (4), VLGAFSDGLAHLDNLK (3-4), VNVDEVGGEALGR (3-4)
HPP 40	14	25	EFTPPVQAAYQK (4-5), FFESFGDLSTPDAVMGNPK (4-5), GTFATLSELHCDK (3-4), KVLGAFSDGLAHLDNLK (4-5), LHVDPENFR (3-4), LLGNVLVCVLAHHFGK (3-5), LLVVYPWTQR (3-5), SAVTALWGK (4-5), VHLTPEEK (3-4), VLGAFSDGLAHLDNLK (3-5), VNVDEVGGEALGR (4-5), VVAGVANALAHK (4-5)
HPP 40	14	26	EFTPPVQAAYQK (3), FFESFGDLSTPDAVMGNPK (3-4), GTFATLSELHCDK (3), KVLGAFSDGLAHLDNLK (3), LLGNVLVCVLAHHFGK (3-4), LLVVYPWTQR (3), SAVTALWGK (3), VHLTPEEK (3), VLGAFSDGLAHLDNLK (3-4), VNVDEVGGEALGR (3), VVAGVANALAHK (3-4)
HPP 40	14	27	FFESFGDLSTPDAVMGNPK (3), LHVDPENFR (3), LLVVYPWTQR (3), SAVTALWGK (3), VHLTPEEK (3), VLGAFSDGLAHLDNLK (3), VNVDEVGGEALGR (3), VVAGVANALAHK (3)
HPP 40	14	28	EFTPPVQAAYQK (5), FFESFGDLSTPDAVMGNPK (4-5), GTFATLSELHCDK (5), KVLGAFSDGLAHLDNLK (5), LLGNVLVCVLAHHFGK (5), LLVVYPWTQR (5), SAVTALWGK (5), VHLTPEEK (4-5), VNVDEVGGEALGR (4-5)
HPP 40	14	29	EFTPPVQAAYQK (5), FFESFGDLSTPDAVMGNPK (4-5), GTFATLSELHCDK (5), LHVDPENFR (5), LLGNVLVCVLAHHFGK (4-5), LLVVYPWTQR (5), VLGAFSDGLAHLDNLK (4), VNVDEVGGEALGR (5)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 40	14	30	EFTPPVQAAYQK (5), FFESFGDLSTPDAVMGNPK (5), KVLGAFSDGLAHLDNLK (5), LLVVYPWTQR (5), SAVTALWGK (5), VLGAFSDGLAHLDNLK (5), VNVDEVGGEALGR (5)
HPP 40	15	14	EFTPPVQAAYQK (12)
HPP 40	15	15	EFTPPVQAAYQK (18-19), FFESFGDLSTPDAVMGNPK (17-20), LLGNVLVCVLAHHFGK (19), LLVVYPWTQR (17, 19, 20), SAVTALWGK (19), VHLTPEEK (17-20), VLGAFSDGLAHLDNLK (17, 19), VVAGVANALAHK (18)
HPP 40	15	16	FFESFGDLSTPDAVMGNPK (12-13, 16, 17), LLVVYPWTQR (12), VNVDEVGGEALGR (12)
HPP 40	15	17	KVLGAFSDGLAHLDNLK (12), LLGNVLVCVLAHHFGK (10), VHLTPEEK (12), VNVDEVGGEALGR (11-12)
HPP 40	15	18	FFESFGDLSTPDAVMGNPK (8-9), GTFATLSELHCDK (8), LLGNVLVCVLAHHFGK (9), LLVVYPWTQR (8, 10), SAVTALWGK (8-9), VLGAFSDGLAHLDNLK (8-9), VNVDEVGGEALGR (8-12), VVAGVANALAHK (9)
HPP 40	15	19	EFTPPVQAAYQK (10), FFESFGDLSTPDAVMGNPK (8-10), GTFATLSELHCDK (8-9), KVLGAFSDGLAHLDNLK (9), LLGNVLVCVLAHHFGK (9, 11, 12), LLVVYPWTQR (11), SAVTALWGK (8, 10), VLGAFSDGLAHLDNLK (8-9), VNVDEVGGEALGR (9-10), VVAGVANALAHK (8-9)
HPP 40	15	24	LLVVYPWTQR (4), VHLTPEEK (4)
HPP 40	16	17	EFTPPVQAAYQK (12-13, 19), FFESFGDLSTPDAVMGNPK (12, 14, 19), GTFATLSELHCDK (12-13, 19), KVLGAFSDGLAHLDNLK (12), LLGNVLVCVLAHHFGK (11-12, 19), LLVVYPWTQR (12, 19, 20), SAVTALWGK (12, 19), VHLTPEEK (19), VLGAFSDGLAHLDNLK (11, 14, 19), VNVDEVGGEALGR (11-14, 18, 19), VVAGVANALAHK (12, 19, 20)
HPP 40	16	18	EFTPPVQAAYQK (8), FFESFGDLSTPDAVMGNPK (8), GTFATLSELHCDK (7-8), LLVVYPWTQR (8), VLGAFSDGLAHLDNLK (8), VNVDEVGGEALGR (7), VVAGVANALAHK (11)
HPP 40	16	19	EFTPPVQAAYQK (7), FFESFGDLSTPDAVMGNPK (7, 11), GTFATLSELHCDK (7), KVLGAFSDGLAHLDNLK (7), LLGNVLVCVLAHHFGK (7-8), LLVVYPWTQR (7-8), SAVTALWGK (7), VLGAFSDGLAHLDNLK (7), VNVDEVGGEALGR (7), VVAGVANALAHK (7)
HPP 40	16	20	FFESFGDLSTPDAVMGNPK (7), VNVDEVGGEALGR (7)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 40	16	21	EFTPPVQAAYQK (7), GTFATLSELHCDK (7), LLVVYPWTQR (8), VVAGVANALAHK (7)
HPP 40	17	17	EFTPPVQAAYQK (12), FFESFGDLSTPDAVMGNPK (12-13), GTFATLSELHCDK (12), KVLGAFSDGLAHLDNLK (12), LLGNVLVCVLAHHFGK (12), LLVVYPWTQR (13), VNVDEVGGEALGR (10-12), VVAGVANALAHK (12-13)
HPP 40	17	18	EFTPPVQAAYQK (7-8), FFESFGDLSTPDAVMGNPK (7-8), GTFATLSELHCDK (8), LHVDPENFR (8), LLGNVLVCVLAHHFGK (7-8), LLVVYPWTQR (7-8), SAVTALWGK (8), VLGAFSDGLAHLDNLK (7-8), VNVDEVGGEALGR (7-8), VVAGVANALAHK (8)
HPP 40	17	19	FFESFGDLSTPDAVMGNPK (8), SAVTALWGKVNVDEVGGEALGR (8), VVAGVANALAHK (8)
HPP 40	17	20	EFTPPVQAAYQK (7), FFESFGDLSTPDAVMGNPK (6-7, 9), GTFATLSELHCDK (8), LLGNVLVCVLAHHFGK (7), LLVVYPWTQR (7), SAVTALWGK (7-8), VHLTPEEK (7), VLGAFSDGLAHLDNLK (7), VNVDEVGGEALGR (7-8, 10)
HPP 40	17	21	FFESFGDLSTPDAVMGNPK (7), GTFATLSELHCDK (7), LLVVYPWTQR (7)
HPP 40	17	22	GTFATLSELHCDK (5)
HPP 40	17	23	VHLTPEEK (5)
HPP 40	17	24	FFESFGDLSTPDAVMGNPK (4), LLVVYPWTQR (3), VLGAFSDGLAHLDNLK (4), VVAGVANALAHK (3)
HPP 40	17	26	FFESFGDLSTPDAVMGNPK (3)
HPP 40	18	17	EFTPPVQAAYQK (11), FFESFGDLSTPDAVMGNPK (11), LLVVYPWTQR (10-11), VNVDEVGGEALGR (10, 12)
HPP 40	18	18	FFESFGDLSTPDAVMGNPK (7-8), GTFATLSELHCDK (8), LLGNVLVCVLAHHFGK (7-8), LLVVYPWTQR (7-8), VLGAFSDGLAHLDNLK (7-8), VVAGVANALAHK (7-8)
HPP 40	18	19	EFTPPVQAAYQK (8), FFESFGDLSTPDAVMGNPK (8), GTFATLSELHCDK (8), LHVDPENFR (8), LLVVYPWTQR (8), VLGAFSDGLAHLDNLK (8), VNVDEVGGEALGR (8)
HPP 40	18	20	VVAGVANALAHK (6)
HPP 40	18	22	LLGNVLVCVLAHHFGK (5), LLVVYPWTQR (5), VNVDEVGGEALGR (5), VVAGVANALAHK (5)
HPP 40	18	23	FFESFGDLSTPDAVMGNPK (5), VLGAFSDGLAHLDNLK (5), VNVDEVGGEALGR (5)

Table 3			
Protein	**CEX**	**RP1**	**Tryptic Sequence (RP2 fractions)**
HPP 40	18	24	GTFATLSELHCDK (3), VNVDEVGGEALGR (3-4)
HPP 40	18	26	LLVVYPWTQR (4)
HPP 40	18	29	LLVVYPWTQR (4), VNVDEVGGEALGR (4), VVAGVANALAHK (4)
HPP 40	18	30	LLVVYPWTQR (4), VNVDEVGGEALGR (4)
HPP 41	1	5	AATVGSLAGQPLQER (18)
HPP 41	8	22	WELALGR (8), WVQTLSEQVQEELLSSQVTQELR (8)
HPP 41	9	18	AATVGSLAGQPLQER (10), LGPLVEQGR (10), LKSWFEPLVEDMQR (10), SWFEPLVEDMQR (11)
HPP 41	9	19	AATVGSLAGQPLQER (8, 12), AKLEEQAQQIR (10-13), LEEQAQQIR (10-13), LGPLVEQGR (10-11), LQAEAFQAR (8, 13), QWAGLVEK (12), SWFEPLVEDMQR (10-13), VQAAVGTSAAPVPSDNH (8-13)
HPP 41	9	20	KVEQAVETEPEPELR (16), WVQTLSEQVQEELLSSQVTQELR (9, 11, 15, 16)
HPP 41	9	21	AKLEEQAQQIR (8-9), LEEQAQQIR (8-9), LGPLVEQGR (7-9), LKSWFEPLVEDMQR (9), LQAEAFQAR (8), QWAGLVEK (8), SWFEPLVEDMQR (8-9), VQAAVGTSAAPVPSDNH (7-8), WVQTLSEQVQEELLSSQVTQELR (9)
HPP 41	9	22	AATVGSLAGQPLQER (6), AKLEEQAQQIR (6), LKSWFEPLVEDMQR (7), LQAEAFQAR (5-6), QWAGLVEK (7), VQAAVGTSAAPVPSDNH (6-7)
HPP 41	10	17	AKLEEQAQQIR (10-11), LGPLVEQGR (10-11), VQAAVGTSAAPVPSDNH (10-11)
HPP 41	10	19	WVQTLSEQVQEELLSSQVTQELR (12)
HPP 41	10	20	AATVGSLAGQPLQER (7-8), AKLEEQAQQIR (7-9), LAVYQAGAR (7), LEEQAQQIR (7), LGPLVEQGR (6-8), LGPLVEQGRVR (7), LQAEAFQAR (6-8), QWAGLVEK (7-9), SWFEPLVEDMQR (8-9), VQAAVGTSAAPVPSDNH (6-8), WVQTLSEQVQEELLSSQVTQELR (9)
HPP 41	10	21	AATVGSLAGQPLQER (7-9), AKLEEQAQQIR (9), LDEVKEQVAEVR (9), LEEQAQQIR (9), LGPLVEQGR (8-9), LQAEAFQAR (8-9), QWAGLVEK (8, 10), SWFEPLVEDMQR (8-10), VQAAVGTSAAPVPSDNH (7-8, 10), WVQTLSEQVQEELLSSQVTQELR (13)
HPP 41	10	22	KVEQAVETEPEPELR (9, 11), WVQTLSEQVQEELLSSQVTQELR (8-11)
HPP 41	11	15	AKLEEQAQQIR (16)
HPP 41	11	19	AATVGSLAGQPLQER (8-11), AKLEEQAQQIR (8, 10), LEEQAQQIR (7, 11), LGPLVEQGR (8-10), LQAEAFQAR (8, 12), SWFEPLVEDMQR (10-11), VQAAVGTSAAPVPSDNH (7-9, 11), WVQTLSEQVQEELLSSQVTQELR (13)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 41	11	20	AATVGSLAGQPLQER (7-10), AKLEEQAQQIR (7, 9, 10), LAVYQAGAR (9), LGPLVEQGR (8-10), LQAEAFQAR (8-11), QWAGLVEK (8-11), SWFEPLVEDMQR (8-11), VQAAVGTSAAPVPSDNH (8-9)
HPP 41	11	21	AATVGSLAGQPLQER (9-11), AKLEEQAQQIR (10-11), LEEQAQQIR (11), LGPLVEQGR (11), LQAEAFQAR (9-11), SWFEPLVEDMQR (10-11), VQAAVGTSAAPVPSDNH (9-11), WVQTLSEQVQEELLSSQVTQELR (12-16)
HPP 41	11	22	AKLEEQAQQIR (7), AQAWGER (7), KVEQAVETEPEPELR (12), LEEQAQQIR (7), LQAEAFQAR (7-8), SWFEPLVEDMQR (7), VQAAVGTSAAPVPSDNH (8), WVQTLSEQVQEELLSSQVTQELR (12)
HPP 41	11	23	LEEQAQQIR (7), LGPLVEQGR (7), LQAEAFQAR (6-8), SWFEPLVEDMQR (6, 8)
HPP 41	12	20	AATVGSLAGQPLQER (6-8), AKLEEQAQQIR (7), LAVYQAGAR (8), LGPLVEQGR (6-8), LKSWFEPLVEDMQR (8), LQAEAFQAR (8, 10), QWAGLVEK (7-8, 10), SWFEPLVEDMQR (6-8), VQAAVGTSAAPVPSDNH (6-8), WVQTLSEQVQEELLSSQVTQELR (8-9)
HPP 41	12	21	AATVGSLAGQPLQER (6-8), AKLEEQAQQIR (6-7, 9), KVEQAVETEPEPELR (16), LAVYQAGAR (7-8), LGPLVEQGR (6-8), LQAEAFQAR (6-7, 9), QWAGLVEK (7-8), SWFEPLVEDMQR (7-9), VQAAVGTSAAPVPSDNH (6-7), WVQTLSEQVQEELLSSQVTQELR (14-16)
HPP 41	12	22	AKLEEQAQQIR (6), VQAAVGTSAAPVPSDNH (5-6)
HPP 41	13	19	LAVYQAGAR (9)
HPP 41	13	20	AATVGSLAGQPLQER (8), AKLEEQAQQIR (8-9), LAVYQAGAR (8), LGPLVEQGR (6-9), LQAEAFQAR (6, 8), QWAGLVEK (8), SWFEPLVEDMQR (8-9), VQAAVGTSAAPVPSDNH (8-9)
HPP 41	13	21	KVEQAVETEPEPELR (16), QWAGLVEK (8), SELEEQLTPVAEETR (11), SWFEPLVEDMQR (7-9), WVQTLSEQVQEELLSSQVTQELR (9-10, 12, 13)
HPP 41	13	22	AATVGSLAGQPLQER (7), AKLEEQAQQIR (7), LAVYQAGAR (7), LGPLVEQGR (7), LQAEAFQAR (6-7), QWAGLVEK (7-8), SWFEPLVEDMQR (7-8), VQAAVGTSAAPVPSDNH (8), WVQTLSEQVQEELLSSQVTQELR (10)
HPP 41	13	23	EQVAEVR (11), WVQTLSEQVQEELLSSQVTQELR (11-13)
HPP 41	14	19	LGPLVEQGR (13), LQAEAFQAR (13-14), VQAAVGTSAAPVPSDNH (13)
HPP 41	14	21	LEEQAQQIR (9), LGPLVEQGR (9)
HPP 41	14	22	LEEQAQQIR (7), LGPLVEQGR (7)
HPP 41	14	23	WVQTLSEQVQEELLSSQVTQELR (12)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 41	17	20	AATVGSLAGQPLQER (11-12), AKLEEQAQQIR (11-12), LQAEAFQAR (12)
HPP 41	17	21	AATVGSLAGQPLQER (11, 13, 14), AYKSELEEQLTPVAEETR (10), LAVYQAGAR (9-12, 14, 15), LGADMEDVCGR (13-14), LGPLVEQGR (9-11, 13, 14, 15), LQAEAFQAR (9-10, 12, 15), QWAGLVEK (9), SELEEQLTPVAEETR (9-12), VQAAVGTSAAPVPSDNH (9-11, 14, 15), WELALGR (10-11), WVQTLSEQVQEELLSSQVTQELR (9)
HPP 41	17	22	AATVGSLAGQPLQER (7-8, 10, 12, 13), AKLEEQAQQIR (8, 10), AYKSELEEQLTPVAEETR (8, 11), GEVQAMLGQSTEELR (7, 10), KVEQAVETEPEPELR (9), LAVYQAGAR (8-9, 11), LGADMEDVCGR (7, 9, 10, 11), LGPLVEQGR (8-9, 11, 12), LKSWFEPLVEDMQR (8), LQAEAFQAR (6, 9), QWAGLVEK (9-10), SELEEQLTPVAEETR (9), SWFEPLVEDMQR (9-10), VQAAVGTSAAPVPSDNH (7-8, 10, 11), WELALGR (7, 9), WVQTLSEQVQEELLSSQVTQELR (7-10)
HPP 41	17	23	AATVGSLAGQPLQER (7-8, 10, 11, 12, 13), AKLEEQAQQIR (9-12), AYKSELEEQLTPVAEETR (9-12), FWDYLR (8), GEVQAMLGQSTEELR (7-11), KVEQAVETEPEPELR (7-11), LAVYQAGAR (8-10), LEEQAQQIR (8-9), LGADMEDVCGR (7-11), LGPLVEQGR (8-10), LQAEAFQAR (9-10), QWAGLVEK (8), SELEEQLTPVAEETR (7-12), SWFEPLVEDMQR (9-11), VQAAVGTSAAPVPSDNH (8-10, 12), WELALGR (8-10), WVQTLSEQVQEELLSSQVTQELR (7-11)
HPP 41	17	24	AATVGSLAGQPLQER (6-7), AKLEEQAQQIR (7-8), GEVQAMLGQSTEELR (8), KVEQAVETEPEPELR (7), LAVYQAGAR (6-7), LGADMEDVCGR (7-8), LGPLVEQGR (6-8), LQAEAFQAR (6), QWAGLVEK (6), SELEEQLTPVAEETR (6-8), SWFEPLVEDMQR (6-7), WELALGR (7), WVQTLSEQVQEELLSSQVTQELR (5-7)
HPP 41	17	25	AATVGSLAGQPLQER (7-8), AATVGSLAGQPLQERAQAWGER (8), AKLEEQAQQIR (7), AQAWGERLR (8), GEVQAMLGQSTEELR (7), GLSAIRER (8), KVEQAVETEPEPELR (7), LAVYQAGAR (7-8), LDEVKEQVAEVR (8), LGADMEDVCGR (6-7), LGPLVEQGR (7-8), LQAEAFQAR (6-8), QQTEWQSGQR (7), QWAGLVEK (7-8), SELEEQLTPVAEETR (6-7), SWFEPLVEDMQR (7), VQAAVGTSAAPVPSDNH (7-8), WELALGR (6-8), WVQTLSEQVQEELLSSQVTQELR (7)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 41	17	26	AATVGSLAGQPLQER (5, 8, 9), FWDYLR (8), LAVYQAGAR (5, 7), LGPLVEQGR (5), SELEEQLTPVAEETR (7-8), SWFEPLVEDMQR (7-9), VQAAVGTSAAPVPSDNH (7-9), WELALGR (7-8), WVQTLSEQVQEELLSSQVTQELR (6-8, 10)
HPP 41	17	27	AATVGSLAGQPLQER (7-9), AKLEEQAQQIR (8), KVEQAVETEPEPELR (8), LGPLVEQGR (8-9), LQAEAFQAR (7-8), SELEEQLTPVAEETR (6, 8), VQAAVGTSAAPVPSDNH (8)
HPP 41	17	28	AATVGSLAGQPLQER (7-8), KVEQAVETEPEPELR (7), LAVYQAGAR (7), LGPLVEQGR (7-8), SELEEQLTPVAEETR (7-8), WVQTLSEQVQEELLSSQVTQELR (8)
HPP 41	17	29	AKLEEQAQQIR (7), LAVYQAGAR (7), LGPLVEQGR (7), LQAEAFQAR (7), SELEEQLTPVAEETR (8)
HPP 41	18	21	AATVGSLAGQPLQER (10-11), AKLEEQAQQIR (9), GEVQAMLGQSTEELR (9), KVEQAVETEPEPELR (11), LGPLVEQGR (9), LQAEAFQAR (9, 12), SELEEQLTPVAEETR (11), WVQTLSEQVQEELLSSQVTQELR (8-9)
HPP 41	18	22	AATVGSLAGQPLQER (9), AKLEEQAQQIR (8, 10), ALMDETMKELK (8), AYKSELEEQLTPVAEETR (8), GEVQAMLGQSTEELR (7), LAVYQAGAR (8-10), LEEQAQQIR (9), LGADMEDVCGR (9-10), LGPLVEQGR (8-11), LQAEAFQAR (8-11), SELEEQLTPVAEETR (8-10), SWFEPLVEDMQR (9), VQAAVGTSAAPVPSDNH (8-9), WELALGR (8-10), WVQTLSEQVQEELLSSQVTQELR (7-9)
HPP 41	18	23	AATVGSLAGQPLQER (9, 11), AKLEEQAQQIR (8, 10), GEVQAMLGQSTEELR (8-10), LAVYQAGAR (8, 10), LGPLVEQGR (9, 11), LQAEAFQAR (8), QWAGLVEK (8-10), SELEEQLTPVAEETR (8, 10), SWFEPLVEDMQR (9), VQAAVGTSAAPVPSDNH (7-10), WELALGR (9-10), WVQTLSEQVQEELLSSQVTQELR (7-9)
HPP 41	18	24	AATVGSLAGQPLQER (8), AKLEEQAQQIR (6-7), GEVQAMLGQSTEELR (7), KVEQAVETEPEPELR (6-7), LAVYQAGAR (7-8), LEEQAQQIR (8), LGADMEDVCGR (7-8), LGPLVEQGR (7-8), LQAEAFQAR (8), QWAGLVEK (7), SELEEQLTPVAEETR (6-8), SWFEPLVEDMQR (7), VQAAVGTSAAPVPSDNH (7), WELALGR (7), WVQTLSEQVQEELLSSQVTQELR (6-7)
HPP 41	18	25	AATVGSLAGQPLQER (6), AKLEEQAQQIR (7), FWDYLR (7), LAVYQAGAR (6-8), LGADMEDVCGR (7), LGPLVEQGR (5-8), QWAGLVEK (6-7), SELEEQLTPVAEETR (6-7), VQAAVGTSAAPVPSDNH (6-8), WELALGR (6-8), WVQTLSEQVQEELLSSQVTQELR (7-8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 41	18	26	AATVGSLAGQPLQER (9-10), AKLEEQAQQIR (9), LGADMEDVCGR (8), LGPLVEQGR (8-9), LQAEAFQAR (7-8), QWAGLVEK (7-8), SELEEQLTPVAEETR (6-9), SWFEPLVEDMQR (7-8), VQAAVGTSAAPVPSDNH (9), WELALGR (8), WVQTLSEQVQEELLSSQVTQELR (6-9)
HPP 41	18	27	AATVGSLAGQPLQER (8-9), AYKSELEEQLTPVAEETR (8), KVEQAVETEPEPELR (9), LGPLVEQGR (8), LQAEAFQAR (8, 10), SELEEQLTPVAEETR (7-8), SWFEPLVEDMQR (8), VQAAVGTSAAPVPSDNH (8), WVQTLSEQVQEELLSSQVTQELR (7-8)
HPP 41	18	28	AATVGSLAGQPLQER (7-8), FWDYLR (7), LAVYQAGAR (8), LEEQAQQIR (8), LGPLVEQGR (7), LKSWFEPLVEDMQR (7), LQAEAFQAR (8), QWAGLVEK (8), SELEEQLTPVAEETR (8), VQAAVGTSAAPVPSDNH (7-8), WELALGR (7), WVQTLSEQVQEELLSSQVTQELR (7-8)
HPP 41	18	29	AATVGSLAGQPLQER (6-10), AKLEEQAQQIR (6-9), LAVYQAGAR (7), LGADMEDVCGR (7-8), LGPLVEQGR (6-8), LQAEAFQAR (6-8), SELEEQLTPVAEETR (6, 9), SWFEPLVEDMQR (7-8), VQAAVGTSAAPVPSDNH (7-8), WELALGR (6-7), WVQTLSEQVQEELLSSQVTQELR (7-9)
HPP 41	18	30	AATVGSLAGQPLQER (7), ALMDETMKELK (7), AYKSELEEQLTPVAEETR (7-8), LAVYQAGAR (8), LGADMEDVCGR (7), LGPLVEQGR (7-8), LQAEAFQAR (6-9), LSKELQAAQAR (7), VQAAVGTSAAPVPSDNH (6), WVQTLSEQVQEELLSSQVTQELR (6)
HPP 42	1	11	VSFLSALEEYTK (13-17)
HPP 42	1	12	DEPPQSPWDR (11, 15, 16), DLATVYVDVLK (13), VSFLSALEEYTK (11-14)
HPP 42	1	13	DEPPQSPWDR (17-18), DYVSQFEGSALGK (21), VKDLATVYVDVLK (16-17), VSFLSALEEYTK (9, 13, 16)
HPP 42	1	14	VSFLSALEEYTK (7)
HPP 42	1	15	DEPPQSPWDR (9), VSFLSALEEYTK (9)
HPP 42	1	16	DEPPQSPWDR (7-8), DLATVYVDVLK (7), DYVSQFEGSALGK (8), VKDLATVYVDVLK (7)
HPP 42	1	17	QGLLPVLESFK (16)
HPP 42	1	18	QGLLPVLESFK (12-13), VSFLSALEEYTK (12, 14)
HPP 42	1	19	QGLLPVLESFK (9)
HPP 42	2	6	DYVSQFEGSALGK (12)
HPP 42	2	7	DYVSQFEGSALGK (12)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	2	9	VSFLSALEEYTK (21)
HPP 42	2	10	VSFLSALEEYTK (13-16)
HPP 42	2	11	VSFLSALEEYTK (8, 10, 12, 14, 21)
HPP 42	2	12	QGLLPVLESFK (8)
HPP 42	2	15	DYVSQFEGSALGK (13, 17, 23), LLDNWDSVTSTFSK (19, 23), VSFLSALEEYTK (20)
HPP 42	2	16	LLDNWDSVTSTFSK (23), LREQLGPVTQEFWDNLEK (23)
HPP 42	2	19	LLDNWDSVTSTFSK (10, 12)
HPP 42	2	20	DYVSQFEGSALGK (10)
HPP 42	3	12	VSFLSALEEYTK (7-10)
HPP 42	3	13	VSFLSALEEYTK (8-10)
HPP 42	3	17	DYVSQFEGSALGK (11), LLDNWDSVTSTFSK (11)
HPP 42	3	18	VSFLSALEEYTK (8)
HPP 42	3	19	VSFLSALEEYTK (8)
HPP 42	3	20	DYVSQFEGSALGK (9-10), LLDNWDSVTSTFSK (8)
HPP 42	3	21	DSGRDYVSQFEGSALGK (9), DYVSQFEGSALGK (7-10), EQLGPVTQEFWDNLEK (9-10), LLDNWDSVTSTFSK (8-10), VKDLATVYVDVLK (9)
HPP 42	3	22	DEPPQSPWDR (8), DLATVYVDVLK (8), DYVSQFEGSALGK (7-9), EQLGPVTQEFWDNLEK (8-9), LLDNWDSVTSTFSK (7-9), VKDLATVYVDVLK (8)
HPP 42	3	23	DYVSQFEGSALGK (7, 9), EQLGPVTQEFWDNLEK (9), LLDNWDSVTSTFSK (8-9), LREQLGPVTQEFWDNLEK (9), VKDLATVYVDVLK (7, 9)
HPP 42	4	12	VSFLSALEEYTK (8-9)
HPP 42	4	13	VSFLSALEEYTK (9-10)
HPP 42	4	18	QGLLPVLESFK (8), VSFLSALEEYTK (8)
HPP 42	4	19	DYVSQFEGSALGK (13)
HPP 42	4	20	DYVSQFEGSALGK (9), LLDNWDSVTSTFSK (8)
HPP 42	4	21	DYVSQFEGSALGK (10, 12)
HPP 42	4	22	DLATVYVDVLK (10), DYVSQFEGSALGK (8-10), EQLGPVTQEFWDNLEK (9-10), LREQLGPVTQEFWDNLEK (9-10), VKDLATVYVDVLK (10)
HPP 42	4	23	DEPPQSPWDR (9), DSGRDYVSQFEGSALGK (9), DYVSQFEGSALGK (8-10), EQLGPVTQEFWDNLEK (8), LLDNWDSVTSTFSK (8-10), LREQLGPVTQEFWDNLEK (8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	5	13	VSFLSALEEYTK (9)
HPP 42	5	17	VSFLSALEEYTK (3, 5, 6)
HPP 42	5	20	DYVSQFEGSALGK (8)
HPP 42	5	21	DYVSQFEGSALGK (9-10)
HPP 42	5	22	DYVSQFEGSALGK (7-8)
HPP 42	5	23	DLATVYVDVLK (9), DYVSQFEGSALGK (7-9), EQLGPVTQEFWDNLEK (9), LLDNWDSVTSTFSK (9), QGLLPVLESFK (5), VSFLSALEEYTK (5)
HPP 42	5	24	QGLLPVLESFK (3)
HPP 42	5	25	EQLGPVTQEFWDNLEK (5), LLDNWDSVTSTFSK (5)
HPP 42	5	27	DSGRDYVSQFEGSALGK (4)
HPP 42	5	28	DEPPQSPWDR (7), DLATVYVDVLK (8), DYVSQFEGSALGK (7-8), EQLGPVTQEFWDNLEK (8), LLDNWDSVTSTFSK (7), LREQLGPVTQEFWDNLEK (7-8), VSFLSALEEYTK (7)
HPP 42	5	29	DYVSQFEGSALGK (7-8)
HPP 42	6	11	VSFLSALEEYTK (11-12)
HPP 42	6	12	VSFLSALEEYTK (9)
HPP 42	6	13	VSFLSALEEYTK (10)
HPP 42	6	17	VSFLSALEEYTK (9)
HPP 42	6	19	DYVSQFEGSALGK (10), VSFLSALEEYTK (8)
HPP 42	6	21	DLATVYVDVLK (9-11), DSGRDYVSQFEGSALGK (8, 12), DYVSQFEGSALGK (9, 11, 12)
HPP 42	6	22	DLATVYVDVLK (8-9), DSGRDYVSQFEGSALGK (10), DYVSQFEGSALGK (8-11), EQLGPVTQEFWDNLEK (10), LLDNWDSVTSTFSK (10), LREQLGPVTQEFWDNLEK (10-11), VKDLATVYVDVLK (10), VQPYLDDFQK (8, 10), VSFLSALEEYTK (5)
HPP 42	6	23	DYVSQFEGSALGK (8), EQLGPVTQEFWDNLEK (8), LLDNWDSVTSTFSK (6, 8), LREQLGPVTQEFWDNLEK (7-8), VSFLSALEEYTK (5, 7, 8, 9)
HPP 42	6	24	DLATVYVDVLK (7), DYVSQFEGSALGK (5, 7), LLDNWDSVTSTFSK (7), VKDLATVYVDVLK (7-8)
HPP 42	6	25	DYVSQFEGSALGK (6)
HPP 42	7	10	VSFLSALEEYTK (12)
HPP 42	7	11	VSFLSALEEYTK (12-13)
HPP 42	7	12	VSFLSALEEYTK (9)
HPP 42	7	17	VSFLSALEEYTK (11)
HPP 42	7	18	DYVSQFEGSALGK (9), LLDNWDSVTSTFSK (10)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	7	20	DYVSQFEGSALGK (8, 10), EQLGPVTQEFWDNLEK (8)
HPP 42	7	21	DYVSQFEGSALGK (8-10), LLDNWDSVTSTFSK (9), VSFLSALEEYTK (6)
HPP 42	7	22	DYVSQFEGSALGK (6-7, 9, 10), QLNLKLLDNWDSVTSTFSK (9), VSFLSALEEYTK (4-5)
HPP 42	7	23	DYVSQFEGSALGK (9-10, 12), LLDNWDSVTSTFSK (10, 12), LREQLGPVTQEFWDNLEK (12)
HPP 42	7	24	DYVSQFEGSALGK (7), LLDNWDSVTSTFSK (7)
HPP 42	8	13	VSFLSALEEYTK (7-9)
HPP 42	8	18	ATEHLSTLSEK (6), QGLLPVLESFK (6), VSFLSALEEYTK (5-6)
HPP 42	8	19	QGLLPVLESFK (9), VSFLSALEEYTK (9)
HPP 42	8	20	ATEHLSTLSEK (6), DYVSQFEGSALGK (7), QGLLPVLESFK (6-7), VSFLSALEEYTK (6-7)
HPP 42	8	21	DLATVYVDVLK (8), DSGRDYVSQFEGSALGK (8), DYVSQFEGSALGK (8-10), EQLGPVTQEFWDNLEK (7), LLDNWDSVTSTFSK (9)
HPP 42	8	22	DSGRDYVSQFEGSALGK (7-8), DYVSQFEGSALGK (6-8), EQLGPVTQEFWDNLEK (6-8), LLDNWDSVTSTFSK (6-8), QGLLPVLESFK (6), VKDLATVYVDVLK (7), VSFLSALEEYTK (7), WQEEMELYR (6)
HPP 42	8	23	ATEHLSTLSEK (7), DEPPQSPWDR (7-9), DLATVYVDVLK (8), DSGRDYVSQFEGSALGK (7-10), DYVSQFEGSALGK (7, 9, 10, 11), LLDNWDSVTSTFSK (6-9), LREQLGPVTQEFWDNLEK (8), QGLLPVLESFK (6-8), THLAPYSDELRQR (7), VKDLATVYVDVLK (8), VQPYLDDFQK (7-8, 10), VQPYLDDFQKK (8), VSFLSALEEYTK (6-7), WQEEMELYR (7, 9)
HPP 42	8	24	DEPPQSPWDR (7), DLATVYVDVLK (7-8), DSGRDYVSQFEGSALGK (7), DYVSQFEGSALGK (7-8), EQLGPVTQEFWDNLEK (5-8), LLDNWDSVTSTFSK (5-8), LREQLGPVTQEFWDNLEK (5-8), QGLLPVLESFK (5-6), VKDLATVYVDVLK (7), WQEEMELYR (6-7)
HPP 42	8	25	DYVSQFEGSALGK (7-8), LLDNWDSVTSTFSK (7)
HPP 42	9	11	VSFLSALEEYTK (12)
HPP 42	9	15	VSFLSALEEYTK (10)
HPP 42	9	16	AKPALEDLR (9), ATEHLSTLSEK (9-10), QGLLPVLESFK (9-10), VSFLSALEEYTK (9-10)
HPP 42	9	17	DYVSQFEGSALGK (14-15), LLDNWDSVTSTFSK (12)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	9	18	ATEHLSTLSEK (7), DLATVYVDVLK (9), DSGRDYVSQFEGSALGK (10), DYVSQFEGSALGK (8-10, 12, 13), EQLGPVTQEFWDNLEK (9, 11), LLDNWDSVTSTFSK (8-11), LREQLGPVTQEFWDNLEK (11-12), VSFLSALEEYTK (9, 11, 12)
HPP 42	9	19	DLATVYVDVLK (13), DYVSQFEGSALGK (11-14), EQLGPVTQEFWDNLEK (12-13), LLDNWDSVTSTFSK (13-14), LREQLGPVTQEFWDNLEK (12), QGLLPVLESFK (6, 12), VSFLSALEEYTK (6-7, 12)
HPP 42	9	20	DEPPQSPWDR (11, 13, 14, 15, 16), DLATVYVDVLK (7, 11, 12, 14), DYVSQFEGSALGK (7-10, 12, 13, 15, 16, 17), EQLGPVTQEFWDNLEK (7-8, 10, 11, 12, 13, 14, 15, 16), EQLGPVTQEFWDNLEKETEGLR (13, 15, 16), ETEGLRQEMSK (14-15), LLDNWDSVTSTFSK (7-8, 10, 11, 12, 13, 14, 15, 17), LREQLGPVTQEFWDNLEK (9-11, 13, 14, 15, 16, 17), VKDLATVYVDVLK (12-14, 16), VQPYLDDFQK (8, 13), VSFLSALEEYTK (11), WQEEMELYR (12-16)
HPP 42	9	21	DEPPQSPWDR (14), DLATVYVDVLK (8), DSGRDYVSQFEGSALGK (13-15), DYVSQFEGSALGK (9-15), EQLGPVTQEFWDNLEK (7-8, 13, 14), ETEGLRQEMSK (14), LLDNWDSVTSTFSK (13-14), LREQLGPVTQEFWDNLEK (12-14), VQPYLDDFQK (8, 13, 14), VQPYLDDFQKK (14), WQEEMELYR (8, 14)
HPP 42	9	22	LLDNWDSVTSTFSK (8), VSFLSALEEYTK (8)
HPP 42	9	23	DEPPQSPWDR (8), DLATVYVDVLK (7-8), DLATVYVDVLKDSGR (8), DSGRDYVSQFEGSALGK (8), DYVSQFEGSALGK (7-10), EQLGPVTQEFWDNLEK (7-9), KWQEEMELYR (8), LLDNWDSVTSTFSK (7-9), LREQLGPVTQEFWDNLEK (7-9), VKDLATVYVDVLK (8), VQPYLDDFQKK (8), WQEEMELYR (7, 9)
HPP 42	9	24	DYVSQFEGSALGK (7), EQLGPVTQEFWDNLEK (7), LLDNWDSVTSTFSK (7), LREQLGPVTQEFWDNLEK (7), WQEEMELYR (7)
HPP 42	10	17	VSFLSALEEYTK (8)
HPP 42	10	18	ATEHLSTLSEK (6-7), QGLLPVLESFK (6-7), VSFLSALEEYTK (6-7, 9)
HPP 42	10	19	DLATVYVDVLK (9-10), DYVSQFEGSALGK (8-10, 13), EQLGPVTQEFWDNLEK (8-10), LLDNWDSVTSTFSK (9, 11), LREQLGPVTQEFWDNLEK (10), QGLLPVLESFK (10-11, 13), VKDLATVYVDVLK (10-11), VSFLSALEEYTK (8-11, 13)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	10	20	DLATVYVDVLK (8), DYVSQFEGSALGK (7-8), EQLGPVTQEFWDNLEK (8), LLDNWDSVTSTFSK (8-9), LREQLGPVTQEFWDNLEK (8), QGLLPVLESFK (7-9), VKDLATVYVDVLK (9), VQPYLDDFQK (8), VSFLSALEEYTK (8-9), WQEEMELYR (8)
HPP 42	10	21	DYVSQFEGSALGK (10), LLDNWDSVTSTFSK (9-10), LREQLGPVTQEFWDNLEK (9), QGLLPVLESFK (9-10), VKDLATVYVDVLK (10), VSFLSALEEYTK (8-9)
HPP 42	10	22	DLATVYVDVLK (8-9), DYVSQFEGSALGK (6-8, 10, 11), EQLGPVTQEFWDNLEK (7-10), LLDNWDSVTSTFSK (6-11), LREQLGPVTQEFWDNLEK (7-9, 11), QGLLPVLESFK (7, 9), QKVEPLR (7), THLAPYSDELR (7), VKDLATVYVDVLK (7, 9, 10), VQPYLDDFQK (7), VSFLSALEEYTK (7-8), WQEEMELYR (8, 10)
HPP 42	10	23	DLATVYVDVLK (11), EQLGPVTQEFWDNLEK (10-11), LLDNWDSVTSTFSK (10-11), LREQLGPVTQEFWDNLEK (10), VKDLATVYVDVLK (10-11), VQPYLDDFQK (8, 10)
HPP 42	11	17	ATEHLSTLSEK (9), LEALKENGGAR (8-9), QGLLPVLESFK (8-9), THLAPYSDELR (9), VSFLSALEEYTK (8-10)
HPP 42	11	18	DLATVYVDVLK (9, 11), DYVSQFEGSALGK (9-11), EQLGPVTQEFWDNLEK (9), LLDNWDSVTSTFSK (8-10), LSPLGEEMR (11), QGLLPVLESFK (7-9, 11, 12), VKDLATVYVDVLK (8, 11, 12), VQPYLDDFQK (11), VSFLSALEEYTK (7-11)
HPP 42	11	19	DEPPQSPWDR (13), DSGRDYVSQFEGSALGK (12-13), DYVSQFEGSALGK (9-14), EQLGPVTQEFWDNLEK (9-11, 13), EQLGPVTQEFWDNLEKETEGLR (10), LLDNWDSVTSTFSK (9-13), LREQLGPVTQEFWDNLEK (9-11, 13, 14), QGLLPVLESFK (7, 10, 11, 12, 13, 14, 15), QGLLPVLESFKVSFLSALEEYTK (12), VKDLATVYVDVLK (10-11, 13), VQPYLDDFQK (9, 11), VSFLSALEEYTK (7-10, 12, 13), WQEEMELYR (14)
HPP 42	11	20	DYVSQFEGSALGK (10), LLDNWDSVTSTFSK (10-11), LREQLGPVTQEFWDNLEK (9), QGLLPVLESFK (6, 8, 9, 10, 11), VQPYLDDFQK (10), VSFLSALEEYTK (6, 9, 10)
HPP 42	11	21	DYVSQFEGSALGK (10, 12, 13, 14, 15), EQLGPVTQEFWDNLEK (8-10, 12, 14), LLDNWDSVTSTFSK (8, 10, 12, 13, 14, 15), LREQLGPVTQEFWDNLEK (8-10, 12, 14), QGLLPVLESFK (8-11, 13, 15), VKDLATVYVDVLK (9-13), VQPYLDDFQK (11), VSFLSALEEYTK (6-7, 10, 11, 12, 13, 14), WQEEMELYR (11)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	11	22	DEPPQSPWDR (9, 22), DLATVYVDVLK (10-12), DLEEVK (11-12), DYVSQFEGSALGK (9, 12), EQLGPVTQEFWDNLEK (8-10), EQLGPVTQEFWDNLEKETEGLR (9), LLDNWDSVTSTFSK (10-12), LREQLGPVTQEFWDNLEK (8-9, 11, 12), QGLLPVLESFK (8), VKDLATVYVDVLK (10-11, 13), VQPYLDDFQK (11-12), VSFLSALEEYTK (8), WQEEMELYR (9)
HPP 42	11	23	DYVSQFEGSALGK (8), LLDNWDSVTSTFSK (8)
HPP 42	11	24	DYVSQFEGSALGK (7), EQLGPVTQEFWDNLEK (8), LLDNWDSVTSTFSK (7-8)
HPP 42	12	17	QGLLPVLESFK (8)
HPP 42	12	18	QGLLPVLESFK (7)
HPP 42	12	19	DLATVYVDVLK (13-14), DSGRDYVSQFEGSALGK (9), DYVSQFEGSALGK (12), LLDNWDSVTSTFSK (9-13), LREQLGPVTQEFWDNLEK (14), QGLLPVLESFK (15), VSFLSALEEYTK (7, 9, 11, 13, 15, 17)
HPP 42	12	20	DSGRDYVSQFEGSALGK (8), DYVSQFEGSALGK (7), LLDNWDSVTSTFSK (7), LREQLGPVTQEFWDNLEK (8), QGLLPVLESFK (7, 10), QGLLPVLESFKVSFLSALEEYTK (8), VSFLSALEEYTK (6-8, 10)
HPP 42	12	21	ATEHLSTLSEK (10), DEPPQSPWDR (13), DLATVYVDVLK (9-10), DLATVYVDVLKDSGR (11), DSGRDYVSQFEGSALGK (11-12), DYVSQFEGSALGK (8, 10, 11, 12, 13, 15), EQLGPVTQEFWDNLEK (9-10, 13, 14), KWQEEMELYR (11), LLDNWDSVTSTFSK (8-13), LREQLGPVTQEFWDNLEK (8-15), LSPLGEEMR (13), QGLLPVLESFK (8, 10, 12, 13, 14), THLAPYSDELR (10), VKDLATVYVDVLK (8-13, 15), VQPYLDDFQK (8-9, 13, 14), VQPYLDDFQKK (11-12), VSFLSALEEYTK (7-10, 13, 16), WQEEMELYR (11-13)
HPP 42	12	22	DLATVYVDVLK (8), DYVSQFEGSALGK (7, 9), QGLLPVLESFK (8), VKDLATVYVDVLK (7), VSFLSALEEYTK (8)
HPP 42	12	23	EQLGPVTQEFWDNLEK (8), LLDNWDSVTSTFSK (9), LREQLGPVTQEFWDNLEK (8)
HPP 42	13	16	VSFLSALEEYTK (8)
HPP 42	13	18	DLATVYVDVLK (9), DYVSQFEGSALGK (11), EQLGPVTQEFWDNLEK (9), QGLLPVLESFK (7, 12), VKDLATVYVDVLK (8), VQPYLDDFQK (11), VSFLSALEEYTK (7, 9, 10, 11, 12)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	13	19	ATEHLSTLSEK (9, 13), DEPPQSPWDR (8), DLATVYVDVLK (9), DSGRDYVSQFEGSALGK (10), DYVSQFEGSALGK (9, 13), EQLGPVTQEFWDNLEK (9, 12), LLDNWDSVTSTFSK (9-10), LREQLGPVTQEFWDNLEK (10), QGLLPVLESFK (9, 11), VKDLATVYVDVLK (8, 10), VQPYLDDFQKK (8, 10), VSFLSALEEYTK (8-9, 11, 12, 13)
HPP 42	13	20	DLATVYVDVLK (8), DYVSQFEGSALGK (8-9), EQLGPVTQEFWDNLEK (8), LLDNWDSVTSTFSK (7-9), LREQLGPVTQEFWDNLEK (8-9), QGLLPVLESFK (7-9), VQPYLDDFQK (8), VSFLSALEEYTK (7-8)
HPP 42	13	21	ATEHLSTLSEK (10), DEPPQSPWDR (8-10), DSGRDYVSQFEGSALGK (8-9), DYVSQFEGSALGK (7-12, 14), EQLGPVTQEFWDNLEK (8, 10, 11, 13), LLDNWDSVTSTFSK (8-10, 14), LREQLGPVTQEFWDNLEK (10, 13), LSPLGEEMR (13), QGLLPVLESFK (9-10, 13), QKLHELQEK (13), THLAPYSDELR (10), VEPLRAELQEGAR (13), VKDLATVYVDVLK (8, 10, 13), VQPYLDDFQK (7, 10), VQPYLDDFQKK (9), VSFLSALEEYTK (8-10, 13, 14, 15), WQEEMELYR (8, 10, 13)
HPP 42	13	22	DEPPQSPWDR (7, 9), DLATVYVDVLK (9), DYVSQFEGSALGK (7-10, 12), EQLGPVTQEFWDNLEK (8-9), EQLGPVTQEFWDNLEKETEGLR (8), LLDNWDSVTSTFSK (7-8), LREQLGPVTQEFWDNLEK (8, 10), LSPLGEEMR (8), QGLLPVLESFK (9), VKDLATVYVDVLK (7-10), VQPYLDDFQK (9-10), VSFLSALEEYTK (7-9), WQEEMELYR (7-10)
HPP 42	13	23	DLATVYVDVLK (8-10), DYVSQFEGSALGK (9-10), EQLGPVTQEFWDNLEK (8, 10), LLDNWDSVTSTFSK (7, 9, 12), LREQLGPVTQEFWDNLEK (8), QGLLPVLESFK (8-9), VKDLATVYVDVLK (7), VQPYLDDFQK (8), VSFLSALEEYTK (7-9), WQEEMELYR (8-9)
HPP 42	13	24	DYVSQFEGSALGK (7-8), EQLGPVTQEFWDNLEK (8), LLDNWDSVTSTFSK (8), VQPYLDDFQK (7)
HPP 42	14	15	VSFLSALEEYTK (10-11)
HPP 42	14	16	QGLLPVLESFK (9), VSFLSALEEYTK (14)
HPP 42	14	17	AKPALEDLR (15, 18), ATEHLSTLSEK (15-21), DEPPQSPWDR (15, 18), DLATVYVDVLK (15, 17), DSGRDYVSQFEGSALGK (16, 18, 21), DYVSQFEGSALGK (15-18, 20), EQLGPVTQEFWDNLEK (14, 17, 18, 19, 20), LLDNWDSVTSTFSK (16-19), LREQLGPVTQEFWDNLEK (14-15, 17, 18, 19, 20), LSPLGEEMR (18, 20, 21), QGLLPVLESFK (14, 16, 17, 18), THLAPYSDELR (17-20), VKDLATVYVDVLK (17), VQPYLDDFQK (20), VSFLSALEEYTK (15-21), WQEEMELYR (17, 19)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	14	18	AKPALEDLR (9, 12, 13), ATEHLSTLSEK (9-15), DEPPQSPWDR (10-12), DLATVYVDVLK (10-14), DSGRDYVSQFEGSALGK (14-15), DYVSQFEGSALGK (10-13, 15, 16), EQLGPVTQEFWDNLEK (8-16), EQLGPVTQEFWDNLEKETEGLR (9), KWQEEMELYR (11), LEALKENGGAR (15), LLDNWDSVTSTFSK (9-16), LREQLGPVTQEFWDNLEK (10-15), LSPLGEEMR (10-12, 15), QGLLPVLESFK (8-16, 19), THLAPYSDELR (11-14, 16), VEPLRAELQEGAR (15), VKDLATVYVDVLK (9, 11, 12, 13, 14, 15), VQPYLDDFQK (11-13, 15), VQPYLDDFQKK (15), VSFLSALEEYTK (8-9, 11, 12, 13, 14, 15, 16, 19), WQEEMELYR (11-16)
HPP 42	14	19	AKPALEDLR (11, 14, 15, 17), ATEHLSTLSEK (13-18), DEPPQSPWDR (13-14, 16, 17, 18), DLATVYVDVLK (14-18), DSGRDYVSQFEGSALGK (13, 15), DYVSQFEGSALGK (10, 12, 15, 16, 17, 18, 19), EQLGPVTQEFWDNLEK (14, 16, 17, 18, 19), LEALKENGGAR (15), LLDNWDSVTSTFSK (11, 15, 16, 17, 18), LREQLGPVTQEFWDNLEK (11, 15, 16, 18), LSPLGEEMR (11-17), QGLLPVLESFK (9, 11, 12, 13, 14, 15, 16, 17, 20, 21), THLAPYSDELR (13-16, 18), VKDLATVYVDVLK (14-18), VQPYLDDFQK (12-14, 16, 17, 18, 19), VQPYLDDFQKK (16), VSFLSALEEYTK (9-11, 14, 15, 16, 17, 18, 19, 20, 21), WQEEMELYR (14-18)
HPP 42	14	20	AHVDALR (10, 12), AKPALEDLR (11, 13), ATEHLSTLSEK (10-16), DEPPQSPWDR (10, 12), DLATVYVDVLK (8, 10, 12), DSGRDYVSQFEGSALGK (13-15), DYVSQFEGSALGK (8-15), EQLGPVTQEFWDNLEK (8, 10, 11, 13, 14), EQLGPVTQEFWDNLEKETEGLR (14), KWQEEMELYR (12-13), LEALKENGGAR (10, 16), LLDNWDSVTSTFSK (9-15), LREQLGPVTQEFWDNLEK (9-12, 14, 15, 16), LSPLGEEMR (10-17), QGLLPVLESFK (9-13, 15, 16, 17), QKLHELQEK (14, 16), THLAPYSDELR (10, 12, 13, 15, 16), VKDLATVYVDVLK (10-11, 13, 14, 15), VQPYLDDFQK (9, 11, 12, 15, 16), VQPYLDDFQKK (14), VSFLSALEEYTK (8-14, 17), WQEEMELYR (12-13, 16)
HPP 42	14	21	DLATVYVDVLK (8), DYVSQFEGSALGK (8, 11, 12, 13, 14, 16), EQLGPVTQEFWDNLEK (8, 10, 11, 12), LLDNWDSVTSTFSK (8, 10, 11, 12, 13, 14, 15, 16), LREQLGPVTQEFWDNLEK (10-12, 16), QGLLPVLESFK (8, 11, 13, 15), THLAPYSDELR (13), VQPYLDDFQK (13), VSFLSALEEYTK (8, 10, 11, 12, 13, 15, 16, 17)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	14	22	AKPALEDLR (7), DEPPQSPWDR (8), DLATVYVDVLK (7-8), DYVSQFEGSALGK (7-8), EQLGPVTQEFWDNLEK (7-9), LLDNWDSVTSTFSK (7-9), LREQLGPVTQEFWDNLEK (7, 9), LSPLGEEMR (7), QGLLPVLESFK (7-11), THLAPYSDELR (7-8), VSFLSALEEYTK (7-12), WQEEMELYR (8)
HPP 42	14	23	ATEHLSTLSEK (8), DLATVYVDVLK (8-9), DYVSQFEGSALGK (7-8, 11, 12), EQLGPVTQEFWDNLEK (8-9, 11, 12), LLDNWDSVTSTFSK (8-11), LREQLGPVTQEFWDNLEK (8-9, 12), LSPLGEEMR (8), QGLLPVLESFK (6-9, 11), THLAPYSDELR (8), VKDLATVYVDVLK (9), VQPYLDDFQK (9), VSFLSALEEYTK (7-11), WQEEMELYR (8-9)
HPP 42	14	24	DLATVYVDVLK (7), DYVSQFEGSALGK (6-8), EQLGPVTQEFWDNLEK (6, 8), LLDNWDSVTSTFSK (6-8), LREQLGPVTQEFWDNLEK (6), QGLLPVLESFK (5, 7), VSFLSALEEYTK (6-8), WQEEMELYR (6-7)
HPP 42	14	25	AHVDALR (7), DLATVYVDVLK (6-7), DYVSQFEGSALGK (6-8), EQLGPVTQEFWDNLEK (6-8), LHELQEK (7), LLDNWDSVTSTFSK (6-8), LREQLGPVTQEFWDNLEK (6), QGLLPVLESFK (6-8), VSFLSALEEYTK (6-8), WQEEMELYR (7)
HPP 42	14	26	ATEHLSTLSEK (6), DYVSQFEGSALGK (6), LLDNWDSVTSTFSK (6), VSFLSALEEYTK (6)
HPP 42	14	27	EQLGPVTQEFWDNLEK (6), QGLLPVLESFK (6), VSFLSALEEYTK (5-7)
HPP 42	14	28	VSFLSALEEYTK (7)
HPP 42	15	9	DLATVYVDVLK (8)
HPP 42	15	15	AHVDALR (12), AKPALEDLR (11), ATEHLSTLSEK (11-12), LEALKENGGAR (12-13), QGLLPVLESFK (10-12, 16, 18, 19), VSFLSALEEYTK (10-12, 14, 15, 17, 19)
HPP 42	15	16	ATEHLSTLSEK (8, 16, 17), DYVSQFEGSALGK (13-14, 16), EQLGPVTQEFWDNLEK (12, 14, 15, 16), LLDNWDSVTSTFSK (12-14, 16), LREQLGPVTQEFWDNLEK (12, 14, 15), LSPLGEEMR (16), QGLLPVLESFK (9, 14), VSFLSALEEYTK (8-10, 12, 13, 14, 17), WQEEMELYR (13, 15)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	15	17	AKPALEDLR (8-9), ATEHLSTLSEK (8-9, 11, 12, 13), DEPPQSPWDR (9, 12), DLATVYVDVLK (8-9, 11), DSGRDYVSQFEGSALGK (8), DYVSQFEGSALGK (8-11, 13), EQLGPVTQEFWDNLEK (8-12), KWQEEMELYR (9), LEALKENGGAR (10), LLDNWDSVTSTFSK (8-11), LREQLGPVTQEFWDNLEK (11), LSPLGEEMR (8-11), QGLLPVLESFK (7-12), THLAPYSDELR (8-9, 11, 12), VKDLATVYVDVLK (8-12), VQPYLDDFQK (8, 10, 11), VSFLSALEEYTK (7-12), WQEEMELYR (8, 11)
HPP 42	15	18	AHVDALR (9-11), AKPALEDLR (9, 12), AKVQPYLDDFQK (8), ATEHLSTLSEK (7-13), DEPPQSPWDR (8-9, 11), DLATVYVDVLK (9), DSGRDYVSQFEGSALGK (9, 11, 12), DYVSQFEGSALGK (7-13), EQLGPVTQEFWDNLEK (10), LEALKENGGAR (8-9, 12), LHELQEK (10), LLDNWDSVTSTFSK (7-10, 12), LSPLGEEMR (7, 10, 11, 13), QGLLPVLESFK (7-10), QGLLPVLESFKVSFLSALEEYTK (9), QKLHELQEK (8-9, 12), THLAPYSDELR (8-10, 13), THLAPYSDELRQR (8-9), VEPLRAELQEGAR (9), VKDLATVYVDVLK (7, 10, 11, 12), VQPYLDDFQK (9-13), VQPYLDDFQKK (8-9), VSFLSALEEYTK (6-11), VSFLSALEEYTKK (9), WQEEMELYR (8-9, 11)
HPP 42	15	19	AHVDALR (11, 17), AHVDALRTHLAPYSDELR (14), AKPALEDLR (10-12, 17), AKPALEDLRQGLLPVLESFK (13), ATEHLSTLSEK (9-13, 16, 17, 18, 19, 20, 21), DEPPQSPWDR (11-14, 16, 18), DEPPQSPWDRVK (13), DLATVYVDVLK (11-12, 14, 16, 17), DSGRDYVSQFEGSALGK (14-15), DYVSQFEGSALGK (10-16, 18, 21, 22), EQLGPVTQEFWDNLEK (9, 11, 12, 16, 17, 18), EQLGPVTQEFWDNLEKETEGLR (10, 12, 17, 18), KWQEEMELYR (13-14, 16), LEALKENGGAR (12-15, 17, 18, 20), LHELQEK (11, 16, 17, 18), LLDNWDSVTSTFSK (9-19), LREQLGPVTQEFWDNLEK (12-15, 17, 18), LSPLGEEMR (10-11, 16, 17, 18, 20), QGLLPVLESFK (7, 9, 10, 11, 12, 13, 15, 16, 17, 18), QGLLPVLESFKVSFLSALEEYTK (12-15), QKLHELQEK (12, 15, 18), THLAPYSDELR (10-11, 14, 15, 16, 18, 19, 20), THLAPYSDELRQR (13-15), VEPLRAELQEGAR (10, 15, 18), VKDLATVYVDVLK (10-19), VQPYLDDFQK (10-11, 13, 14, 16, 17, 18), VQPYLDDFQKK (10, 12, 13, 15, 17, 18, 20), VSFLSALEEYTK (7-8, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 22), VSFLSALEEYTKK (14-15), WQEEMELYR (10-14, 16, 17, 18, 19)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	15	20	AHVDALR (7-9, 14), AKPALEDLR (7, 9, 10, 11), ATEHLSTLSEK (7-12, 14), DEPPQSPWDR (8-10, 12), DLATVYVDVLK (7-9, 11, 12), DSGRDYVSQFEGSALGK (11-12, 14), DYVSQFEGSALGK (7-12), EQLGPVTQEFWDNLEK (7-12), EQLGPVTQEFWDNLEKETEGLR (10-11), KWQEEMELYR (10-11), LEALKENGGAR (11), LHELQEK (7-8, 10, 11, 12, 14), LLDNWDSVTSTFSK (7-12, 14), LREQLGPVTQEFWDNLEK (7, 9, 10, 11, 12, 14), LSPLGEEMR (7-12, 14), QGLLPVLESFK (7-11, 14), QLNLKLLDNWDSVTSTFSK (11-12), THLAPYSDELR (7-10), VKDLATVYVDVLK (9-11, 14), VQPYLDDFQK (8-11), VQPYLDDFQKK (10-11), VSFLSALEEYTK (7-12, 14), WQEEMELYR (7-12)
HPP 42	15	21	ATEHLSTLSEK (9, 11, 12, 13), DEPPQSPWDR (9-10, 12), DLATVYVDVLK (8-11), DSGRDYVSQFEGSALGK (11-12), DYVSQFEGSALGK (7-13), EQLGPVTQEFWDNLEK (8-13), LLDNWDSVTSTFSK (8, 10, 11, 12), LREQLGPVTQEFWDNLEK (10-13), LSPLGEEMR (10-13), QGLLPVLESFK (7, 11, 12), THLAPYSDELR (7-8, 10, 11, 12, 13), VKDLATVYVDVLK (9-11), VQPYLDDFQK (8-9), VSFLSALEEYTK (8-13), WQEEMELYR (8, 11, 12, 13)
HPP 42	15	22	AKPALEDLR (9), ATEHLSTLSEK (7-11), DEPPQSPWDR (9), DLATVYVDVLK (7-9), DSGRDYVSQFEGSALGK (10), DYVSQFEGSALGK (7, 9, 10, 11, 13), EQLGPVTQEFWDNLEK (7-10), KWQEEMELYR (7, 9), LLDNWDSVTSTFSK (7-10), LREQLGPVTQEFWDNLEK (10), LSPLGEEMR (7, 9, 10), QGLLPVLESFK (7-10), QKVEPLR (9), THLAPYSDELR (7, 10, 11), VKDLATVYVDVLK (9-10), VQPYLDDFQK (7), VSFLSALEEYTK (6-11), WQEEMELYR (7-9)
HPP 42	15	23	AHVDALR (7, 11), AKPALEDLR (7, 10), ATEHLSTLSEK (7-12), DEPPQSPWDR (7-9), DLATVYVDVLK (8-10), DSGRDYVSQFEGSALGK (10-11), DYVSQFEGSALGK (7-12), EQLGPVTQEFWDNLEK (7-10), EQLGPVTQEFWDNLEKETEGLR (10-11), ETEGLRQEMSK (7), KWQEEMELYR (7, 9), LEALKENGGAR (9, 12), LHELQEK (7, 10), LLDNWDSVTSTFSK (7-11), LREQLGPVTQEFWDNLEK (7, 11), LSPLGEEMR (7-8, 10), QGLLPVLESFK (7-11), THLAPYSDELR (7-9, 11), VKDLATVYVDVLK (10-11), VQPYLDDFQK (7-8, 10, 12), VSFLSALEEYTK (7-12), WQEEMELYR (7-11)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	15	24	AKPALEDLR (6), ATEHLSTLSEK (6-8), DEPPQSPWDR (6-7), DLATVYVDVLK (5, 7, 8, 9), DYVSQFEGSALGK (5-8, 10, 12), EQLGPVTQEFWDNLEK (5-9), EQLGPVTQEFWDNLEKETEGLR (6), LLDNWDSVTSTFSK (5-9), LREQLGPVTQEFWDNLEK (6-7, 9), LSPLGEEMR (7-8, 10), QGLLPVLESFK (5, 7, 9, 10, 12), THLAPYSDELR (7), VQPYLDDFQK (5-7), VSFLSALEEYTK (5-8, 11, 12), WQEEMELYR (6-8)
HPP 42	15	25	DYVSQFEGSALGK (6, 9), EQLGPVTQEFWDNLEK (7-8), LLDNWDSVTSTFSK (6-7), LSPLGEEMR (7), QGLLPVLESFK (6-8), VSFLSALEEYTK (5-6, 8, 9, 10)
HPP 42	15	26	ATEHLSTLSEK (5-6), DLATVYVDVLK (6), DYVSQFEGSALGK (4-6), LLDNWDSVTSTFSK (5, 7), LREQLGPVTQEFWDNLEK (5-7), LSPLGEEMR (6), QGLLPVLESFK (4, 6, 8), VSFLSALEEYTK (4-8), WQEEMELYR (6)
HPP 42	15	27	DYVSQFEGSALGK (6-7), LLDNWDSVTSTFSK (6), QGLLPVLESFK (4, 6, 7), VSFLSALEEYTK (5-6)
HPP 42	15	28	ATEHLSTLSEK (7), LLDNWDSVTSTFSK (7), QGLLPVLESFK (7), VKDLATVYVDVLK (7), VSFLSALEEYTK (7)
HPP 42	15	29	DYVSQFEGSALGK (7), EQLGPVTQEFWDNLEK (7), LREQLGPVTQEFWDNLEK (7), LSPLGEEMR (7), QGLLPVLESFK (7), VSFLSALEEYTK (7)
HPP 42	16	17	ATEHLSTLSEK (17), QGLLPVLESFK (17, 19), VSFLSALEEYTK (11, 17, 18, 19)
HPP 42	16	18	QGLLPVLESFK (7-8), VSFLSALEEYTK (9)
HPP 42	16	19	DLATVYVDVLK (12-13), QGLLPVLESFK (6-7), VSFLSALEEYTK (6-7)
HPP 42	16	20	ATEHLSTLSEK (11), DLATVYVDVLK (8-9), DYVSQFEGSALGK (8-13), EQLGPVTQEFWDNLEK (7-12), LLDNWDSVTSTFSK (8-10), LREQLGPVTQEFWDNLEK (10-11), LSPLGEEMR (9-10), QGLLPVLESFK (5, 7, 8, 9, 10), THLAPYSDELR (8), VQPYLDDFQK (8), VSFLSALEEYTK (5, 7, 8, 10, 11), WQEEMELYR (8-12)
HPP 42	16	21	ATEHLSTLSEK (7-8), DLATVYVDVLK (7), DYVSQFEGSALGK (6-9), EQLGPVTQEFWDNLEK (7-8), LLDNWDSVTSTFSK (6-8), LREQLGPVTQEFWDNLEK (8), LSPLGEEMR (8), QGLLPVLESFK (6-8), THLAPYSDELR (8), VQPYLDDFQK (7-8), VSFLSALEEYTK (5-8), WQEEMELYR (7-8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	16	22	AKPALEDLR (8), DSGRDYVSQFEGSALGK (8), DYVSQFEGSALGK (8, 10), EQLGPVTQEFWDNLEK (7), LEALKENGGAR (8), LLDNWDSVTSTFSK (8), QGLLPVLESFK (8), VQPYLDDFQK (8), VSFLSALEEYTK (7-8, 10)
HPP 42	16	23	AHVDALR (8), ATEHLSTLSEK (7-8), DEPPQSPWDR (7), DLATVYVDVLK (7-8), DYVSQFEGSALGK (5, 7, 8, 9), EQLGPVTQEFWDNLEK (7-8), KWQEEMELYR (7), LLDNWDSVTSTFSK (7-8), LREQLGPVTQEFWDNLEK (7-8), LSPLGEEMR (7-8), QGLLPVLESFK (7-8), VKDLATVYVDVLK (8), VQPYLDDFQK (7-8), VSFLSALEEYTK (5, 8), WQEEMELYR (7-8)
HPP 42	16	24	AKPALEDLR (5), ATEHLSTLSEK (4-6), DYVSQFEGSALGK (5, 7), EQLGPVTQEFWDNLEK (4-5, 7), LLDNWDSVTSTFSK (5, 7), LREQLGPVTQEFWDNLEK (4-7), LSPLGEEMR (5-6), QGLLPVLESFK (4-7), THLAPYSDELR (4-5), VSFLSALEEYTK (4-7), WQEEMELYR (5-7)
HPP 42	16	25	AHVDALR (6), AKPALEDLR (5), DYVSQFEGSALGK (5-7), EQLGPVTQEFWDNLEK (5-7), LLDNWDSVTSTFSK (5-6), LSPLGEEMR (5-7), QGLLPVLESFK (5-7), THLAPYSDELR (6), VQPYLDDFQK (7), VSFLSALEEYTK (5-7), WQEEMELYR (5-6)
HPP 42	16	26	DLATVYVDVLK (7), DYVSQFEGSALGK (6-8), EQLGPVTQEFWDNLEK (7-8), QGLLPVLESFK (5, 8), VQPYLDDFQK (7-8), VSFLSALEEYTK (6-8), WQEEMELYR (7)
HPP 42	16	27	DYVSQFEGSALGK (6-7), EQLGPVTQEFWDNLEK (6), LLDNWDSVTSTFSK (6-7), VSFLSALEEYTK (5-8), WQEEMELYR (7)
HPP 42	16	28	DYVSQFEGSALGK (6-8), EQLGPVTQEFWDNLEK (5-7), LLDNWDSVTSTFSK (6), QGLLPVLESFK (6-7), VQPYLDDFQK (7), VSFLSALEEYTK (5-8), WQEEMELYR (6-7)
HPP 42	16	29	DYVSQFEGSALGK (6-7), LLDNWDSVTSTFSK (6), QGLLPVLESFK (6), VSFLSALEEYTK (5-7)
HPP 42	16	30	ATEHLSTLSEK (6), DYVSQFEGSALGK (6-7), EQLGPVTQEFWDNLEK (6-7), LREQLGPVTQEFWDNLEK (6), LSPLGEEMR (6), QGLLPVLESFK (6-7), VQPYLDDFQK (6-7), VSFLSALEEYTK (6-7), WQEEMELYR (6)
HPP 42	17	18	ATEHLSTLSEK (6), QGLLPVLESFK (6-7), THLAPYSDELR (6), VSFLSALEEYTK (6-7)
HPP 42	17	19	DYVSQFEGSALGK (11-12), EQLGPVTQEFWDNLEK (11), QGLLPVLESFK (8, 11), VSFLSALEEYTK (9-10, 12)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	17	20	AKPALEDLR (8), ATEHLSTLSEK (8), DEPPQSPWDR (8-9), DLATVYVDVLK (8), DYVSQFEGSALGK (8-9), EQLGPVTQEFWDNLEK (8-9), LLDNWDSVTSTFSK (9), LREQLGPVTQEFWDNLEK (11), LSPLGEEMR (8), QGLLPVLESFK (6, 8, 9, 11, 12), THLAPYSDELR (9), VKDLATVYVDVLK (8, 12), VQPYLDDFQK (8), VSFLSALEEYTK (5-6, 8, 9, 11)
HPP 42	17	21	AHVDALR (10-11, 13), AKPALEDLR (9-10, 13), ATEHLSTLSEK (7, 9, 10, 11, 12, 13, 14), DLATVYVDVLK (9-12), DSGRDYVSQFEGSALGK (9-11, 14), DYVSQFEGSALGK (8-13, 15, 16), EQLGPVTQEFWDNLEK (9-12), EQLGPVTQEFWDNLEKETEGLR (10-15), ETEGLRQEMSK (11), KWQEEMELYR (12-13), LEALKENGGAR (14), LHELQEK (13), LLDNWDSVTSTFSK (7, 9, 10, 11, 12, 13), LREQLGPVTQEFWDNLEK (7, 9, 10, 11, 12, 13), LSPLGEEMR (9-12), QGLLPVLESFK (5, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16), QKLHELQEK (14), THLAPYSDELR (7, 9, 10, 11, 12, 13), VEPLRAELQEGAR (15), VKDLATVYVDVLK (10-16), VQPYLDDFQK (9-12, 14, 15), VQPYLDDFQKK (10-11, 13, 14), VSFLSALEEYTK (6-15, 17), WQEEMELYR (9-12, 14, 15, 16)
HPP 42	17	22	AKPALEDLR (7), AKPALEDLRQGLLPVLESFK (8), ATEHLSTLSEK (7-8), DEPPQSPWDR (8), DLATVYVDVLK (8-9), DSGRDYVSQFEGSALGK (8), DYVSQFEGSALGK (7-9), EQLGPVTQEFWDNLEK (7-9), KWQEEMELYR (8), LLDNWDSVTSTFSK (8-9), LREQLGPVTQEFWDNLEK (8-9), QGLLPVLESFK (3, 7, 8, 9, 10), QGLLPVLESFKVSFLSALEEYTK (8), QKLHELQEK (8), QLNLKLLDNWDSVTSTFSK (8), VKDLATVYVDVLK (7-8), VQPYLDDFQK (9), VSFLSALEEYTK (3-5, 8, 9, 10, 11), WQEEMELYR (7-8)
HPP 42	17	23	AKPALEDLR (8), ATEHLSTLSEK (6-8), DEPPQSPWDR (7-8), DLATVYVDVLK (8), DSGRDYVSQFEGSALGK (7), DYVSQFEGSALGK (6-9), EQLGPVTQEFWDNLEK (6-8), KWQEEMELYR (8), LEALKENGGAR (8), LLDNWDSVTSTFSK (6-10), LREQLGPVTQEFWDNLEK (6-9), QGLLPVLESFK (6-8, 10), THLAPYSDELR (7-9), VKDLATVYVDVLK (7-8), VQPYLDDFQK (6-8), VSFLSALEEYTK (4, 6, 7, 8, 9, 10), WQEEMELYR (6-9)
HPP 42	17	24	ATEHLSTLSEK (5-6), DLATVYVDVLK (5-7), DSGRDYVSQFEGSALGK (5), DYVSQFEGSALGK (4-8), EQLGPVTQEFWDNLEK (4-8), EQLGPVTQEFWDNLEKETEGLR (5), LLDNWDSVTSTFSK (4-7), LREQLGPVTQEFWDNLEK (4-7), LSPLGEEMR (5-7), QGLLPVLESFK (4-8), THLAPYSDELR (5-7), VEPLRAELQEGAR (5), VKDLATVYVDVLK (5-7), VQPYLDDFQK (4-7), VQPYLDDFQKK (5), VSFLSALEEYTK (2, 4, 5, 6, 7, 8), VSFLSALEEYTKK (5), WQEEMELYR (5-6)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	17	25	AHVDALR (6), AKPALEDLR (4, 6, 7), ATEHLSTLSEK (5-7), DEPPQSPWDR (6), DLATVYVDVLK (5-7), DSGRDYVSQFEGSALGK (4-6), DYVSQFEGSALGK (4-8, 10), EQLGPVTQEFWDNLEK (5-7), EQLGPVTQEFWDNLEKETEGLR (6), LEALKENGGAR (6), LLDNWDSVTSTFSK (4-8), LREQLGPVTQEFWDNLEK (5-7), LSPLGEEMR (5-7), QGLLPVLESFK (4-7), QKVEPLR (6), VKDLATVYVDVLK (6-7), VQPYLDDFQK (5-7), VQPYLDDFQKK (4-5), VSFLSALEEYTK (3-8), WQEEMELYR (5-7)
HPP 42	17	26	AKPALEDLR (5-6), ATEHLSTLSEK (4-5, 7), DSGRDYVSQFEGSALGK (6-7), DYVSQFEGSALGK (3-8), EQLGPVTQEFWDNLEK (8), LEALKENGGAR (6-7), LLDNWDSVTSTFSK (5-8), LREQLGPVTQEFWDNLEK (8), LSPLGEEMR (5, 7, 8), QGLLPVLESFK (5), THLAPYSDELR (5), VKDLATVYVDVLK (6-7), VQPYLDDFQK (4-5), VQPYLDDFQKK (7), VSFLSALEEYTK (3-5, 7, 8, 9), WQEEMELYR (5-8)
HPP 42	17	27	ATEHLSTLSEK (6-7), DEPPQSPWDR (7), DLATVYVDVLK (6-7), DSGRDYVSQFEGSALGK (7), DYVSQFEGSALGK (5-8), EQLGPVTQEFWDNLEK (5-7), LLDNWDSVTSTFSK (5-8), LREQLGPVTQEFWDNLEK (6-7), LSPLGEEMR (6-8), QGLLPVLESFK (5-8), THLAPYSDELR (7), VKDLATVYVDVLK (6), VQPYLDDFQK (6-7), VSFLSALEEYTK (4-8)
HPP 42	17	28	ATEHLSTLSEK (7), DLATVYVDVLK (5-6), DYVSQFEGSALGK (6-8), EQLGPVTQEFWDNLEK (5-8), LLDNWDSVTSTFSK (7), LREQLGPVTQEFWDNLEK (7), LSPLGEEMR (6-7), QGLLPVLESFK (5-10), VSFLSALEEYTK (4-9), WQEEMELYR (7)
HPP 42	17	29	ATEHLSTLSEK (7), DLATVYVDVLK (7), DYVSQFEGSALGK (6-7), EQLGPVTQEFWDNLEK (6-8), LLDNWDSVTSTFSK (6-7), LREQLGPVTQEFWDNLEK (6-7), QGLLPVLESFK (6-7), THLAPYSDELR (6-7), VQPYLDDFQK (8), VSFLSALEEYTK (6-7, 9)
HPP 42	17	30	DLATVYVDVLK (7), DYVSQFEGSALGK (6-7), EQLGPVTQEFWDNLEK (6-8), LLDNWDSVTSTFSK (6-7), LREQLGPVTQEFWDNLEK (7), QGLLPVLESFK (6, 8), THLAPYSDELR (6), VQPYLDDFQK (7), VSFLSALEEYTK (6-8), WQEEMELYR (7)
HPP 42	18	12	VSFLSALEEYTK (9)
HPP 42	18	18	QGLLPVLESFK (6), VSFLSALEEYTK (6)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	18	19	DSGRDYVSQFEGSALGK (9), DYVSQFEGSALGK (11), EQLGPVTQEFWDNLEK (11), LLDNWDSVTSTFSK (10), LREQLGPVTQEFWDNLEK (11), QGLLPVLESFK (10-11), VSFLSALEEYTK (8-9, 11)
HPP 42	18	20	ATEHLSTLSEK (7, 9), DEPPQSPWDR (7), DLATVYVDVLK (8), DLATVYVDVLKDSGR (8), DSGRDYVSQFEGSALGK (7-8), DYVSQFEGSALGK (7-9), EQLGPVTQEFWDNLEK (7-9), EQLGPVTQEFWDNLEKETEGLR (8), LLDNWDSVTSTFSK (7-9), LREQLGPVTQEFWDNLEK (8), QGLLPVLESFK (7-8, 12), THLAPYSDELR (7), VKDLATVYVDVLK (7-8), VQPYLDDFQK (9), VSFLSALEEYTK (5-7, 9, 10, 12), WQEEMELYR (7)
HPP 42	18	21	ATEHLSTLSEK (8-10), DEPPQSPWDR (8-10), DLATVYVDVLK (8-10), DYVSQFEGSALGK (7-9, 11, 12), EQLGPVTQEFWDNLEK (8-11), LLDNWDSVTSTFSK (8-11), LREQLGPVTQEFWDNLEK (8-10), LSPLGEEMR (8, 10), QGLLPVLESFK (7-12), THLAPYSDELR (8-9), VKDLATVYVDVLK (8, 10), VQPYLDDFQK (7-10), VSFLSALEEYTK (5, 7, 8, 9, 10, 11, 12, 13), WQEEMELYR (8-11)
HPP 42	18	22	AKPALEDLR (6, 8, 9), AKPALEDLRQGLLPVLESFK (8), ATEHLSTLSEK (6, 8), DEPPQSPWDR (7), DLATVYVDVLK (6-9), DSGRDYVSQFEGSALGK (7-8), DYVSQFEGSALGK (6-10), EQLGPVTQEFWDNLEK (6-7), KLNTQ (7), KWQEEMELYR (7-8), LAEYHAK (7), LLDNWDSVTSTFSK (6-9), LREQLGPVTQEFWDNLEK (6-7), LSPLGEEMR (6-7, 9), QGLLPVLESFK (4-10), THLAPYSDELR (7-10), VEPLRAELQEGAR (7), VKDLATVYVDVLK (6-8), VQPYLDDFQK (6-7, 9), VQPYLDDFQKK (7-8), VSFLSALEEYTK (4-10), VSFLSALEEYTKK (7-8), WQEEMELYR (6-7, 9)
HPP 42	18	23	AKPALEDLR (7), ATEHLSTLSEK (6-9), DEPPQSPWDR (6, 8), DLATVYVDVLK (7-9), DYVSQFEGSALGK (5-7, 9, 10, 11), EQLGPVTQEFWDNLEK (6-9), LLDNWDSVTSTFSK (6-10), LREQLGPVTQEFWDNLEK (6-9), LSPLGEEMR (7-9), QGLLPVLESFK (6, 9, 10), THLAPYSDELR (6-10), VKDLATVYVDVLK (6-9), VQPYLDDFQK (6-7), VSFLSALEEYTK (4-10), WQEEMELYR (6-9)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	18	24	AKPALEDLR (4-5), ATEHLSTLSEK (4-7), DEPPQSPWDR (6), DLATVYVDVLK (4-6), DYVSQFEGSALGK (4-8), EQLGPVTQEFWDNLEK (4-7), EQLGPVTQEFWDNLEKETEGLR (6), LLDNWDSVTSTFSK (4-7), LREQLGPVTQEFWDNLEK (4-6), LSPLGEEMR (4-6, 8), QGLLPVLESFK (2, 4, 5, 6, 7, 8), THLAPYSDELR (4-7), VKDLATVYVDVLK (6), VQPYLDDFQK (7), VSFLSALEEYTK (2, 4, 5, 6, 7, 8), WQEEMELYR (4-7)
HPP 42	18	25	AKPALEDLR (4-5), ATEHLSTLSEK (5-6), DEPPQSPWDR (6-7), DLATVYVDVLK (4-8), DSGRDYVSQFEGSALGK (4-5), DYVSQFEGSALGK (4-7), EQLGPVTQEFWDNLEK (4-8), LLDNWDSVTSTFSK (4-8), LREQLGPVTQEFWDNLEK (5-7), LSPLGEEMR (6-7), QGLLPVLESFK (2-8), THLAPYSDELR (2, 4, 5, 6, 8), VKDLATVYVDVLK (5-6), VQPYLDDFQK (5-8), VQPYLDDFQKK (5), VSFLSALEEYTK (2-9), WQEEMELYR (4-6)
HPP 42	18	26	AKPALEDLRQGLLPVLESFK (5-6), ATEHLSTLSEK (7), DEPPQSPWDR (6-7), DLATVYVDVLK (6-8), DSGRDYVSQFEGSALGK (6), DYVSQFEGSALGK (5-9), EQLGPVTQEFWDNLEK (5-9), LEALKENGGAR (6), LLDNWDSVTSTFSK (5-9), LREQLGPVTQEFWDNLEK (5-9), QGLLPVLESFK (5-9), THLAPYSDELR (5-9), THLAPYSDELRQR (5-6), VKDLATVYVDVLK (6-7), VQPYLDDFQK (6-7), VSFLSALEEYTK (5-10), WQEEMELYR (6-8)
HPP 42	18	27	AKPALEDLR (6), ATEHLSTLSEK (5-8), DEPPQSPWDR (7), DLATVYVDVLK (7), DYVSQFEGSALGK (6-8), EQLGPVTQEFWDNLEK (5-9), LLDNWDSVTSTFSK (5, 7, 8), LREQLGPVTQEFWDNLEK (7-8), LSPLGEEMR (7-8), QGLLPVLESFK (5, 7, 9, 10), VQPYLDDFQK (8), VSFLSALEEYTK (5, 7, 8, 11), WQEEMELYR (7)
HPP 42	18	28	AKPALEDLR (5-6), AKPALEDLRQGLLPVLESFK (7), ATEHLSTLSEK (6-7), DEPPQSPWDR (7), DLATVYVDVLK (5-6), DSGRDYVSQFEGSALGK (7), DYVSQFEGSALGK (5-8), EQLGPVTQEFWDNLEK (5-8), LLDNWDSVTSTFSK (5-8), LREQLGPVTQEFWDNLEK (5-7), LSPLGEEMR (6-8), QGLLPVLESFK (3, 6, 7, 8), QKLHELQEK (7), THLAPYSDELR (6-7), THLAPYSDELRQR (7), VKDLATVYVDVLK (6), VQPYLDDFQK (5-6, 8), VQPYLDDFQKK (7), VSFLSALEEYTK (4-10), WQEEMELYR (6-7)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 42	18	29	AKPALEDLR (5), ATEHLSTLSEK (5-7), DEPPQSPWDR (6), DLATVYVDVLK (7), DSGRDYVSQFEGSALGK (5), DYVSQFEGSALGK (5-7), EQLGPVTQEFWDNLEK (6-7), LLDNWDSVTSTFSK (6-8), LREQLGPVTQEFWDNLEK (7), LSPLGEEMR (7), QGLLPVLESFK (5-9), THLAPYSDELR (5-6), VKDLATVYVDVLK (5-7), VQPYLDDFQK (6-7), VQPYLDDFQKK (5-6), VSFLSALEEYTK (4-9), WQEEMELYR (5-7)
HPP 42	18	30	AKPALEDLR (5-7), AKPALEDLRQGLLPVLESFK (7), ATEHLSTLSEK (6-7), DEPPQSPWDR (5-7), DSGRDYVSQFEGSALGK (6-7), DYVSQFEGSALGK (5-9), EQLGPVTQEFWDNLEK (5-7), LEALKENGGAR (6), LLDNWDSVTSTFSK (5, 7), LREQLGPVTQEFWDNLEK (5-8), LSPLGEEMR (6-7), QGLLPVLESFK (5-7, 9), THLAPYSDELR (5-6), THLAPYSDELRQR (6-7), VQPYLDDFQK (6-7), VQPYLDDFQKK (5-6), VSFLSALEEYTK (5-10), WQEEMELYR (5-7)
HPP 43	9	20	DASGVTFTWTPSSGK (7), DLCGCYSVSSVLPGCAEPWNHGK (7), KGDTFSCMVGHEALPLAFTQK (7), QEPSQGTTTFAVTSILR (7), TFTCTAAYPESK (7), TPLTATLSK (7), WLQGSQELPR (7)
HPP 43	9	23	DASGVTFTWTPSSGK (6), DLCGCYSVSSVLPGCAEPWNHGK (6), QEPSQGTTTFAVTSILR (6), TPLTATLSK (6), WLQGSQELPR (6)
HPP 44	1	11	EPCVESLVSQYFQTVTDYGK (16)
HPP 44	1	15	SKEQLTPLIK (21)
HPP 44	1	16	AGTELVNFLSYFVELGTQPATQ (13-14, 17, 18, 20), KAGTELVNFLSYFVELGTQPATQ (17-18), SKEQLTPLIK (13-17, 20), VKSPELQAEAK (13-15)
HPP 44	1	17	AGTELVNFLSYFVELGTQPATQ (18-20), EPCVESLVSQYFQTVTDYGK (18), EQLTPLIK (18), KAGTELVNFLSYFVELGTQPATQ (18, 20), VKSPELQAEAK (18)
HPP 44	1	18	AGTELVNFLSYFVELGTQPATQ (7, 12, 13, 14, 15, 17, 18, 19, 20, 21, 22, 23, 24), EPCVESLVSQYFQTVTDYGK (7, 9, 10, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22), EQLTPLIK (12-13, 15), KAGTELVNFLSYFVELGTQPATQ (9-10, 12, 13, 14, 15, 16, 17, 18, 20, 21, 22, 23), QAKEPCVESLVSQYFQTVTDYGK (20), SKEQLTPLIK (9-10, 12, 13, 14, 15, 16, 18, 19, 20, 21, 22), SPELQAEAK (17-19, 21), SPELQAEAKSYFEK (13-14), VKSPELQAEAK (13-15, 18)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	1	19	AGTELVNFLSYFVELGTQPATQ (8-9, 11, 12, 13, 14, 16, 17, 20, 21), DLMEK (19-20, 22), EPCVESLVSQYFQTVTDYGK (8-9, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 24), EQLTPLIK (10, 14, 16, 17, 18, 19, 20, 21, 22, 24), KAGTELVNFLSYFVELGTQPATQ (8-11, 13, 14, 15, 16, 17, 20, 21, 22, 24), SKEQLTPLIK (7-8, 10, 11, 14, 16, 17, 18, 20, 21, 22, 23, 24), SPELQAEAK (7-8, 11, 12, 14, 15, 17, 18, 19, 20, 21, 22, 23, 24), SPELQAEAKSYFEK (21), SYFEK (14-15, 17, 18, 19, 20, 21, 22, 24), VKSPELQAEAK (8, 20, 21, 22, 23)
HPP 44	1	20	AGTELVNFLSYFVELGTQPATQ (7-19), EPCVESLVSQYFQTVTDYGK (5, 8, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20), EPCVESLVSQYFQTVTDYGKDLMEK (19), KAGTELVNFLSYFVELGTQPATQ (7-8, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19), SKEQLTPLIK (12-13, 15, 16, 17, 18, 19, 20), SPELQAEAK (18), SPELQAEAKSYFEK (17-18), VKSPELQAEAK (11, 15, 17, 19)
HPP 44	1	21	AGTELVNFLSYFVELGTQPATQ (9), EPCVESLVSQYFQTVTDYGK (8-9), EQLTPLIK (8), SKEQLTPLIK (10), SPELQAEAK (8), VKSPELQAEAK (10)
HPP 44	1	22	AGTELVNFLSYFVELGTQPATQ (6-24), EPCVESLVSQYFQTVTDYGK (6-12, 14, 15, 16, 18), EPCVESLVSQYFQTVTDYGKDLMEK (8-11, 13, 14, 17), EQLTPLIK (7-8), KAGTELVNFLSYFVELGTQPATQ (7-22, 24), QAKEPCVESLVSQYFQTVTDYGK (8-9), SKEQLTPLIK (7-10, 12), SPELQAEAK (8-9), VKSPELQAEAK (8-10)
HPP 44	1	23	AGTELVNFLSYFVELGTQPATQ (20), EPCVESLVSQYFQTVTDYGK (7-9), EPCVESLVSQYFQTVTDYGKDLMEK (8), EQLTPLIK (11), KAGTELVNFLSYFVELGTQPATQ (7-10), QAKEPCVESLVSQYFQTVTDYGK (9), SKEQLTPLIK (7-12), SPELQAEAK (7-8), SYFEK (7-8), VKSPELQAEAK (8-10)
HPP 44	1	24	AGTELVNFLSYFVELGTQPATQ (8), EPCVESLVSQYFQTVTDYGK (8), EQLTPLIK (8), KAGTELVNFLSYFVELGTQPATQ (8-9), SKEQLTPLIK (8-9)
HPP 44	1	25	EQLTPLIK (9), SKEQLTPLIK (8-9), SPELQAEAK (8)
HPP 44	2	1	AGTELVNFLSYFVELGTQPATQ (1-3, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 20, 21), EPCVESLVSQYFQTVTDYGK (1-3, 10), KAGTELVNFLSYFVELGTQPATQ (1-2, 7, 9, 10, 11, 22)
HPP 44	2	3	AGTELVNFLSYFVELGTQPATQ (3, 5, 6, 11, 14), EPCVESLVSQYFQTVTDYGK (17), KAGTELVNFLSYFVELGTQPATQ (6-7, 10, 11, 12, 14, 17, 19)
HPP 44	2	10	EPCVESLVSQYFQTVTDYGK (16-17, 19, 20, 21, 22, 23), SKEQLTPLIK (24), SPELQAEAK (19-20, 22)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	2	11	EPCVESLVSQYFQTVTDYGK (24), VKSPELQAEAK (15)
HPP 44	2	13	EPCVESLVSQYFQTVTDYGK (17, 24)
HPP 44	2	14	EPCVESLVSQYFQTVTDYGK (21-22), SKEQLTPLIK (10)
HPP 44	2	15	AGTELVNFLSYFVELGTQPATQ (20-23), EPCVESLVSQYFQTVTDYGK (18-23), EQLTPLIK (18, 23, 24), KAGTELVNFLSYFVELGTQPATQ (18-23), QAKEPCVESLVSQYFQTVTDYGK (19-21), SKEQLTPLIK (18-21, 23, 24), SPELQAEAK (19, 21), SYFEK (18-20), VKSPELQAEAK (19-20)
HPP 44	2	16	AGTELVNFLSYFVELGTQPATQ (9, 15, 17, 18, 19, 21, 22, 24), EPCVESLVSQYFQTVTDYGK (10, 14, 15, 17, 18, 19, 20, 21, 22, 24), EPCVESLVSQYFQTVTDYGKDLMEK (21), EQLTPLIK (9, 14, 17, 18, 19), KAGTELVNFLSYFVELGTQPATQ (14-24), SKEQLTPLIK (16, 18, 19, 20, 21, 22, 23, 24), SPELQAEAK (16-18), SYFEK (17-18)
HPP 44	2	17	AGTELVNFLSYFVELGTQPATQ (8-11, 19, 20, 21, 22, 23), EPCVESLVSQYFQTVTDYGK (8-9, 18, 19, 20, 21, 22, 23, 24), EQLTPLIK (7-9, 21, 22), KAGTELVNFLSYFVELGTQPATQ (7-9, 18, 19, 20, 21, 22, 23, 24), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (8-9, 19, 20, 21, 22), SPELQAEAK (8, 19, 20, 21, 22), SYFEK (20-21), VKSPELQAEAK (9, 19, 20, 21, 22)
HPP 44	2	18	AGTELVNFLSYFVELGTQPATQ (6-11, 19), EPCVESLVSQYFQTVTDYGK (7-9, 11, 12, 13, 16, 17, 19, 20, 21, 22, 23), EPCVESLVSQYFQTVTDYGKDLMEK (16-17, 22, 23), EQLTPLIK (7, 9, 12, 16, 19, 20, 21, 22), KAGTELVNFLSYFVELGTQPATQ (7-8, 11, 12, 16, 17, 19, 20, 21, 22), SKEQLTPLIK (6-13, 16, 17, 19, 20, 21, 23), SPELQAEAK (7-9, 11, 12, 16, 19, 20, 21), SYFEK (8, 20), VKSPELQAEAK (8-10, 16, 17, 18, 22)
HPP 44	2	19	AGTELVNFLSYFVELGTQPATQ (10-24), EPCVESLVSQYFQTVTDYGK (10-24), EPCVESLVSQYFQTVTDYGKDLMEK (13, 20), EQLTPLIK (10, 14, 21), KAGTELVNFLSYFVELGTQPATQ (10-13, 15, 16, 18, 19, 20, 21, 22, 23), QAKEPCVESLVSQYFQTVTDYGK (12), SKEQLTPLIK (9-16, 19, 20, 21, 22, 24), SPELQAEAK (10-11, 14, 16, 18, 19, 24), VKSPELQAEAK (9, 13, 14, 21, 24)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	2	20	AGTELVNFLSYFVELGTQPATQ (9-17, 20, 21, 22, 23), EPCVESLVSQYFQTVTDYGK (8-17, 21, 22, 23, 24), EPCVESLVSQYFQTVTDYGKDLMEK (8-9, 11, 14, 15, 16, 17, 22, 23), EQLTPLIK (9-11, 14, 15, 16, 21, 22, 23), EQLTPLIKK (11), KAGTELVNFLSYFVELGTQPATQ (8-17, 19, 20, 21, 22, 23, 24), QAKEPCVESLVSQYFQTVTDYGK (9, 22), SKEQLTPLIK (8-13, 15, 16, 17, 21, 23, 24), SPELQAEAK (10, 16), SYFEK (8, 10), VKSPELQAEAK (8-10, 12, 13, 15, 16, 22)
HPP 44	2	21	AGTELVNFLSYFVELGTQPATQ (15, 23), EPCVESLVSQYFQTVTDYGK (8-9, 11, 12, 13, 14, 15, 16, 17, 22, 23, 24), EQLTPLIK (9, 12, 13, 14, 15, 16, 17), KAGTELVNFLSYFVELGTQPATQ (13-15, 17), QAKEPCVESLVSQYFQTVTDYGK (12), SKEQLTPLIK (11-17), SPELQAEAK (9-17), VKSPELQAEAK (9, 12, 13, 14, 15, 16, 17)
HPP 44	2	22	AGTELVNFLSYFVELGTQPATQ (9, 11), EPCVESLVSQYFQTVTDYGK (7-10), KAGTELVNFLSYFVELGTQPATQ (7-8), SKEQLTPLIK (8-11), SPELQAEAK (8-10), VKSPELQAEAK (9-10)
HPP 44	2	23	EPCVESLVSQYFQTVTDYGK (10)
HPP 44	2	25	EPCVESLVSQYFQTVTDYGK (7, 21)
HPP 44	2	30	AGTELVNFLSYFVELGTQPATQ (2, 4)
HPP 44	3	8	AGTELVNFLSYFVELGTQPATQ (7-8, 13, 15, 19), EPCVESLVSQYFQTVTDYGK (1, 3, 4, 6, 9, 11, 13)
HPP 44	3	12	EPCVESLVSQYFQTVTDYGK (10)
HPP 44	3	13	EPCVESLVSQYFQTVTDYGK (9-12)
HPP 44	3	14	KAGTELVNFLSYFVELGTQPATQ (1)
HPP 44	3	15	EPCVESLVSQYFQTVTDYGK (1-2, 8, 11, 17)
HPP 44	3	17	EPCVESLVSQYFQTVTDYGK (10-11, 13), SPELQAEAK (13)
HPP 44	3	18	AGTELVNFLSYFVELGTQPATQ (1, 3), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (8), SPELQAEAK (8), VKSPELQAEAK (8)
HPP 44	3	19	AGTELVNFLSYFVELGTQPATQ (8-15), EPCVESLVSQYFQTVTDYGK (6, 8, 9, 10, 11, 12, 14), EPCVESLVSQYFQTVTDYGKDLMEK (9, 11), EQLTPLIK (9), KAGTELVNFLSYFVELGTQPATQ (8-13), QAKEPCVESLVSQYFQTVTDYGK (8-9), SKEQLTPLIK (8-10), SPELQAEAK (9-10), SYFEK (9), VKSPELQAEAK (9-10)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	3	20	AGTELVNFLSYFVELGTQPATQ (9-15), EPCVESLVSQYFQTVTDYGK (5-14), EPCVESLVSQYFQTVTDYGKDLMEK (9), EQLTPLIK (7-9, 11), KAGTELVNFLSYFVELGTQPATQ (7-12, 14), QAKEPCVESLVSQYFQTVTDYGK (7-8, 10, 11, 13), SKEQLTPLIK (7-10), SPELQAEAK (7-8, 10), SYFEK (7-10), VKSPELQAEAK (7-9)
HPP 44	3	21	AGTELVNFLSYFVELGTQPATQ (9-19, 21, 22, 23, 24), EPCVESLVSQYFQTVTDYGK (8-18, 20, 21, 23), EPCVESLVSQYFQTVTDYGKDLMEK (9-12), EQLTPLIK (9-12), KAGTELVNFLSYFVELGTQPATQ (7-13, 15, 17, 18, 22, 24), QAKEPCVESLVSQYFQTVTDYGK (8-10), SKEQLTPLIK (8-13), SPELQAEAK (9-13), SPELQAEAKSYFEK (12), SYFEK (9-10, 13), VKSPELQAEAK (8, 10, 11, 12)
HPP 44	3	22	AGTELVNFLSYFVELGTQPATQ (7-10, 13, 15, 16, 17, 18, 19, 20, 21), EPCVESLVSQYFQTVTDYGK (7-10), EPCVESLVSQYFQTVTDYGKDLMEK (7-10, 12, 14, 16), EQLTPLIK (8-9), KAGTELVNFLSYFVELGTQPATQ (7-12, 14, 16, 17), QAKEPCVESLVSQYFQTVTDYGK (7-9), SKEQLTPLIK (7-10), SPELQAEAK (8-9), SPELQAEAKSYFEK (9), SYFEK (7, 9), VKSPELQAEAK (7-10)
HPP 44	3	23	AGTELVNFLSYFVELGTQPATQ (8-9), EPCVESLVSQYFQTVTDYGK (7, 9, 10), EPCVESLVSQYFQTVTDYGKDLMEK (8-10), KAGTELVNFLSYFVELGTQPATQ (7-10), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (7-10), SPELQAEAKSYFEK (9), VKSPELQAEAK (9)
HPP 44	3	24	EPCVESLVSQYFQTVTDYGK (5-7, 9), EQLTPLIK (8), SKEQLTPLIK (6-8), VKSPELQAEAK (7-8)
HPP 44	4	3	AGTELVNFLSYFVELGTQPATQ (15), EPCVESLVSQYFQTVTDYGK (7, 11)
HPP 44	4	12	EPCVESLVSQYFQTVTDYGK (9, 12)
HPP 44	4	13	EPCVESLVSQYFQTVTDYGK (9-13), QAKEPCVESLVSQYFQTVTDYGK (10), SPELQAEAK (9)
HPP 44	4	14	AGTELVNFLSYFVELGTQPATQ (8, 14, 15, 16, 17)
HPP 44	4	16	EPCVESLVSQYFQTVTDYGK (10-11)
HPP 44	4	17	EPCVESLVSQYFQTVTDYGK (14)
HPP 44	4	18	AGTELVNFLSYFVELGTQPATQ (9-10), EPCVESLVSQYFQTVTDYGK (8-10), KAGTELVNFLSYFVELGTQPATQ (8-9), SKEQLTPLIK (9), SPELQAEAK (9)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	4	19	AGTELVNFLSYFVELGTQPATQ (7-12), EPCVESLVSQYFQTVTDYGK (8-13), EQLTPLIK (8-10), KAGTELVNFLSYFVELGTQPATQ (8-12), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (9-11), SPELQAEAK (9-10), VKSPELQAEAK (8, 10)
HPP 44	4	20	AGTELVNFLSYFVELGTQPATQ (7-15), EPCVESLVSQYFQTVTDYGK (6-15), EPCVESLVSQYFQTVTDYGKDLMEK (8-10, 14), EQLTPLIK (8, 10, 11, 12, 14), KAGTELVNFLSYFVELGTQPATQ (7-12), QAKEPCVESLVSQYFQTVTDYGK (7-8, 13), SKEQLTPLIK (7-14), SPELQAEAK (8-9), VKSPELQAEAK (7-11, 13, 14)
HPP 44	4	21	AGTELVNFLSYFVELGTQPATQ (10-13, 15, 16, 17, 20, 23, 24), EPCVESLVSQYFQTVTDYGK (9-18), EPCVESLVSQYFQTVTDYGKDLMEK (11-12), EQLTPLIK (9-10, 13), KAGTELVNFLSYFVELGTQPATQ (9-20), QAKEPCVESLVSQYFQTVTDYGK (11), SKEQLTPLIK (9-15), SPELQAEAK (9-10, 12), SYFEK (12), VKSPELQAEAK (9-12)
HPP 44	4	22	AGTELVNFLSYFVELGTQPATQ (8-9, 11), EPCVESLVSQYFQTVTDYGK (7-12), EPCVESLVSQYFQTVTDYGKDLMEK (8-9), EQLTPLIK (8-12), KAGTELVNFLSYFVELGTQPATQ (8-10), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (7-12), SPELQAEAK (8, 13), SYFEK (10), VKSPELQAEAK (8, 10)
HPP 44	4	23	AGTELVNFLSYFVELGTQPATQ (9, 11, 12, 13), DLMEK (12-13), EPCVESLVSQYFQTVTDYGK (6-13), EQLTPLIK (8-13), KAGTELVNFLSYFVELGTQPATQ (8-14), QAKEPCVESLVSQYFQTVTDYGK (9), SKEQLTPLIK (8-14), SPELQAEAK (10-13), SYFEK (12-13), VKSPELQAEAK (8-12)
HPP 44	4	24	AGTELVNFLSYFVELGTQPATQ (8, 10, 11, 13), EPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (7-8), VKSPELQAEAK (8, 11)
HPP 44	4	27	AGTELVNFLSYFVELGTQPATQ (6)
HPP 44	5	9	SKEQLTPLIK (12), SPELQAEAK (12), VKSPELQAEAK (12)
HPP 44	5	11	SKEQLTPLIK (10)
HPP 44	5	13	EPCVESLVSQYFQTVTDYGK (10, 12, 13)
HPP 44	5	14	EPCVESLVSQYFQTVTDYGK (8)
HPP 44	5	16	EPCVESLVSQYFQTVTDYGK (14, 17)
HPP 44	5	17	EPCVESLVSQYFQTVTDYGK (7, 13)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	5	20	AGTELVNFLSYFVELGTQPATQ (7-14, 16, 20, 21, 22), EPCVESLVSQYFQTVTDYGK (5, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 21, 22), EQLTPLIK (7-8), KAGTELVNFLSYFVELGTQPATQ (7-10, 14), SKEQLTPLIK (7-8), SPELQAEAK (7, 9)
HPP 44	5	21	AGTELVNFLSYFVELGTQPATQ (8-10, 12, 13, 14, 16), EPCVESLVSQYFQTVTDYGK (7-13), EQLTPLIK (8, 10), KAGTELVNFLSYFVELGTQPATQ (8-11), SKEQLTPLIK (7-11), SPELQAEAK (7-11), SYFEK (10), VKSPELQAEAK (7, 9, 10, 11)
HPP 44	5	22	AGTELVNFLSYFVELGTQPATQ (7-12, 14, 15, 17, 20), EPCVESLVSQYFQTVTDYGK (7-17, 19, 20, 21, 22, 24), EQLTPLIK (7-9), KAGTELVNFLSYFVELGTQPATQ (7-8), SKEQLTPLIK (7), SPELQAEAK (7, 9), SYFEK (7), VKSPELQAEAK (7, 9)
HPP 44	5	23	AGTELVNFLSYFVELGTQPATQ (8-9), EPCVESLVSQYFQTVTDYGK (5, 7, 8, 9, 10), EQLTPLIK (5, 7, 9), KAGTELVNFLSYFVELGTQPATQ (7, 9, 10), SKEQLTPLIK (4-5, 7, 9), SPELQAEAK (7-9), SPELQAEAKSYFEK (9), VKSPELQAEAK (7, 9)
HPP 44	5	24	AGTELVNFLSYFVELGTQPATQ (4-6, 8, 9), EPCVESLVSQYFQTVTDYGK (2-5, 7, 8, 9), EPCVESLVSQYFQTVTDYGKDLMEK (5), EQLTPLIK (3), EQLTPLIKK (4), KAGTELVNFLSYFVELGTQPATQ (4-6), QAKEPCVESLVSQYFQTVTDYGK (4-6), SKEQLTPLIK (3-5), SPELQAEAK (7, 9), SYFEK (7), VKSPELQAEAK (4)
HPP 44	5	25	AGTELVNFLSYFVELGTQPATQ (4-6, 8, 9, 10, 15, 22, 23), EPCVESLVSQYFQTVTDYGK (2-10, 14), EPCVESLVSQYFQTVTDYGKDLMEK (5), EQLTPLIK (7-8), KAGTELVNFLSYFVELGTQPATQ (4-8, 10, 11, 14, 15), QAKEPCVESLVSQYFQTVTDYGK (4, 7, 10), SKEQLTPLIK (4-5, 8, 9), SPELQAEAK (8), VKSPELQAEAK (7, 9)
HPP 44	5	26	AGTELVNFLSYFVELGTQPATQ (4, 6, 7, 10), EPCVESLVSQYFQTVTDYGK (4-7), EQLTPLIK (4-5), KAGTELVNFLSYFVELGTQPATQ (4-6), SKEQLTPLIK (4), SPELQAEAK (4-6), VKSPELQAEAK (4-5)
HPP 44	5	27	AGTELVNFLSYFVELGTQPATQ (6-8), EPCVESLVSQYFQTVTDYGK (5-10, 12, 13, 15), EPCVESLVSQYFQTVTDYGKDLMEK (4), EQLTPLIK (5, 7), KAGTELVNFLSYFVELGTQPATQ (4), QAKEPCVESLVSQYFQTVTDYGK (4), SKEQLTPLIK (4-5, 7), SPELQAEAK (4-6), VKSPELQAEAK (4, 6)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	5	28	AGTELVNFLSYFVELGTQPATQ (9), EPCVESLVSQYFQTVTDYGK (5-8), KAGTELVNFLSYFVELGTQPATQ (7-8), SKEQLTPLIK (6, 8, 9), VKSPELQAEAK (7-8)
HPP 44	5	29	AGTELVNFLSYFVELGTQPATQ (8), EPCVESLVSQYFQTVTDYGK (7-8), EQLTPLIK (8), SKEQLTPLIK (7-9), SPELQAEAK (8), VKSPELQAEAK (8)
HPP 44	5	30	AGTELVNFLSYFVELGTQPATQ (5, 19, 20)
HPP 44	6	7	AGTELVNFLSYFVELGTQPATQ (7, 9, 13), EPCVESLVSQYFQTVTDYGK (1-2, 4, 7, 9, 19)
HPP 44	6	8	AGTELVNFLSYFVELGTQPATQ (2, 8), EPCVESLVSQYFQTVTDYGK (1)
HPP 44	6	12	EPCVESLVSQYFQTVTDYGK (9, 11)
HPP 44	6	13	EPCVESLVSQYFQTVTDYGK (10)
HPP 44	6	17	EPCVESLVSQYFQTVTDYGK (10-12), SKEQLTPLIK (10-11)
HPP 44	6	18	AGTELVNFLSYFVELGTQPATQ (9-10), EPCVESLVSQYFQTVTDYGK (8-13), EQLTPLIK (8, 10), EQLTPLIKK (9), KAGTELVNFLSYFVELGTQPATQ (8-11), QAKEPCVESLVSQYFQTVTDYGK (9), SKEQLTPLIK (9-11), SYFEK (10), VKSPELQAEAK (9-10)
HPP 44	6	19	AGTELVNFLSYFVELGTQPATQ (9-12), EPCVESLVSQYFQTVTDYGK (7-10, 12, 13), EPCVESLVSQYFQTVTDYGKDLMEK (12), EQLTPLIK (9-10), KAGTELVNFLSYFVELGTQPATQ (9, 11), SKEQLTPLIK (8-11), SPELQAEAK (8-10), VKSPELQAEAK (8-9, 11, 12)
HPP 44	6	20	AGTELVNFLSYFVELGTQPATQ (7-13, 15, 17, 19, 22, 24), EPCVESLVSQYFQTVTDYGK (6-24), EQLTPLIK (7-10), KAGTELVNFLSYFVELGTQPATQ (7-11, 13, 14, 16, 19, 24), SKEQLTPLIK (9), SPELQAEAK (10-11), VKSPELQAEAK (7-11)
HPP 44	6	21	AGTELVNFLSYFVELGTQPATQ (8, 10), EPCVESLVSQYFQTVTDYGK (6-12), EPCVESLVSQYFQTVTDYGKDLMEK (8), EQLTPLIK (9-10), KAGTELVNFLSYFVELGTQPATQ (8-12), SKEQLTPLIK (6-12), SPELQAEAK (7-11), SYFEK (7), VKSPELQAEAK (7, 9, 10, 11, 12)
HPP 44	6	22	AGTELVNFLSYFVELGTQPATQ (6-11, 13, 14), EPCVESLVSQYFQTVTDYGK (4-14, 17, 18), EPCVESLVSQYFQTVTDYGKDLMEK (7-10), EQLTPLIK (5-8), KAGTELVNFLSYFVELGTQPATQ (6-11), QAKEPCVESLVSQYFQTVTDYGK (7), SKEQLTPLIK (5-11), SPELQAEAK (7-8), VKSPELQAEAK (6, 11)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	6	23	AGTELVNFLSYFVELGTQPATQ (5-6, 9), EPCVESLVSQYFQTVTDYGK (3, 5, 6, 7, 8), EPCVESLVSQYFQTVTDYGKDLMEK (6-8), EQLTPLIK (8), KAGTELVNFLSYFVELGTQPATQ (5-8), QAKEPCVESLVSQYFQTVTDYGK (6-7), SKEQLTPLIK (6-8), SPELQAEAK (6, 8), SYFEK (5, 7), VKSPELQAEAK (5-8)
HPP 44	6	24	AGTELVNFLSYFVELGTQPATQ (5-7), EPCVESLVSQYFQTVTDYGK (3-8), EQLTPLIK (5), KAGTELVNFLSYFVELGTQPATQ (5), SKEQLTPLIK (3-8), SPELQAEAK (5-6), VKSPELQAEAK (4, 7, 8)
HPP 44	6	25	AGTELVNFLSYFVELGTQPATQ (1-2, 5, 6, 7), EPCVESLVSQYFQTVTDYGK (1-11, 13, 14, 17, 20, 21, 22, 23), EPCVESLVSQYFQTVTDYGKDLMEK (6), KAGTELVNFLSYFVELGTQPATQ (5), SKEQLTPLIK (4), SYFEK (5), VKSPELQAEAK (4-5)
HPP 44	7	9	SKEQLTPLIK (10)
HPP 44	7	16	EPCVESLVSQYFQTVTDYGK (13), KAGTELVNFLSYFVELGTQPATQ (12-13), SKEQLTPLIK (12-13)
HPP 44	7	17	AGTELVNFLSYFVELGTQPATQ (11, 13, 14, 15), EPCVESLVSQYFQTVTDYGK (11-18), KAGTELVNFLSYFVELGTQPATQ (11-12, 14, 15, 16, 17), SKEQLTPLIK (10-16), SPELQAEAK (11-17), VKSPELQAEAK (11-17)
HPP 44	7	18	AGTELVNFLSYFVELGTQPATQ (11), EPCVESLVSQYFQTVTDYGK (8-12), EPCVESLVSQYFQTVTDYGKDLMEK (11), EQLTPLIK (10-12), KAGTELVNFLSYFVELGTQPATQ (8, 11), SKEQLTPLIK (9-11), SPELQAEAK (8-12), VKSPELQAEAK (9, 11, 12)
HPP 44	7	19	AGTELVNFLSYFVELGTQPATQ (9-10, 12, 13, 18), EPCVESLVSQYFQTVTDYGK (8-15, 17, 18), EQLTPLIK (9, 17), KAGTELVNFLSYFVELGTQPATQ (9-10, 13, 16, 17), SKEQLTPLIK (9-13, 15, 17, 18), SPELQAEAK (11-13, 17), VKSPELQAEAK (8-9, 12, 13, 14, 15, 16, 17, 18)
HPP 44	7	20	AGTELVNFLSYFVELGTQPATQ (9, 13), EPCVESLVSQYFQTVTDYGK (7-11), EQLTPLIK (8-9), KAGTELVNFLSYFVELGTQPATQ (8-11), SKEQLTPLIK (7-11), SPELQAEAK (8, 10, 11), VKSPELQAEAK (8-11)
HPP 44	7	21	AGTELVNFLSYFVELGTQPATQ (9, 12, 13, 15, 16, 17), EPCVESLVSQYFQTVTDYGK (8-16), EQLTPLIK (8-9, 11, 12, 13), KAGTELVNFLSYFVELGTQPATQ (8, 11, 12, 13, 16), SKEQLTPLIK (7-12, 14, 15), SPELQAEAK (8, 10, 11, 12, 13, 14), VKSPELQAEAK (7, 9, 10, 12, 15)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	7	22	AGTELVNFLSYFVELGTQPATQ (8-9, 11, 12), EPCVESLVSQYFQTVTDYGK (5-10, 12), EPCVESLVSQYFQTVTDYGKDLMEK (6-10), EQLTPLIK (6, 8, 9), EQLTPLIKK (8), KAGTELVNFLSYFVELGTQPATQ (7-10), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (6-10), SPELQAEAK (5-9), SYFEK (5-7), VKSPELQAEAK (5-10)
HPP 44	7	23	AGTELVNFLSYFVELGTQPATQ (8-10), EPCVESLVSQYFQTVTDYGK (6-11), EQLTPLIK (8-9), KAGTELVNFLSYFVELGTQPATQ (7, 9, 10, 11), QAKEPCVESLVSQYFQTVTDYGK (7), SKEQLTPLIK (6-10), SPELQAEAK (6), VKSPELQAEAK (6-9)
HPP 44	7	24	AGTELVNFLSYFVELGTQPATQ (6-8), EPCVESLVSQYFQTVTDYGK (5-8), EPCVESLVSQYFQTVTDYGKDLMEK (6-7), KAGTELVNFLSYFVELGTQPATQ (6-7), SKEQLTPLIK (5-7), VKSPELQAEAK (5-6)
HPP 44	7	25	EPCVESLVSQYFQTVTDYGK (5-7), EQLTPLIK (7), SKEQLTPLIK (5-7), SPELQAEAK (7)
HPP 44	7	26	EPCVESLVSQYFQTVTDYGK (4-5), SKEQLTPLIK (4-5)
HPP 44	7	27	EPCVESLVSQYFQTVTDYGK (4), SKEQLTPLIK (3-4)
HPP 44	7	28	SKEQLTPLIK (4-5), SPELQAEAK (4, 6), VKSPELQAEAK (6)
HPP 44	8	10	AGTELVNFLSYFVELGTQPATQ (3, 20)
HPP 44	8	13	EPCVESLVSQYFQTVTDYGK (10)
HPP 44	8	16	AGTELVNFLSYFVELGTQPATQ (6, 8, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24), EPCVESLVSQYFQTVTDYGK (7, 9, 10, 11)
HPP 44	8	18	EPCVESLVSQYFQTVTDYGK (7), SKEQLTPLIK (7)
HPP 44	8	19	AGTELVNFLSYFVELGTQPATQ (8, 10), EPCVESLVSQYFQTVTDYGK (6-10), KAGTELVNFLSYFVELGTQPATQ (7-9), QAKEPCVESLVSQYFQTVTDYGK (7-8), SKEQLTPLIK (7-8), SYFEK (7), VKSPELQAEAK (7)
HPP 44	8	20	AGTELVNFLSYFVELGTQPATQ (7, 10, 11, 12), EPCVESLVSQYFQTVTDYGK (6-9), EPCVESLVSQYFQTVTDYGKDLMEK (8), EQLTPLIK (7), KAGTELVNFLSYFVELGTQPATQ (6-10), QAKEPCVESLVSQYFQTVTDYGK (7-8), SKEQLTPLIK (6-8), SPELQAEAK (6), VKSPELQAEAK (8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	8	21	AGTELVNFLSYFVELGTQPATQ (8-10), EPCVESLVSQYFQTVTDYGK (4-12), EPCVESLVSQYFQTVTDYGKDLMEK (8, 11), EQLTPLIK (7, 10), EQLTPLIKK (8), KAGTELVNFLSYFVELGTQPATQ (8-11), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (6-8, 10, 11), SPELQAEAK (6-9, 11), SYFEK (7), VKSPELQAEAK (8, 10)
HPP 44	8	22	AGTELVNFLSYFVELGTQPATQ (5-21, 23, 24), EPCVESLVSQYFQTVTDYGK (4-24), EPCVESLVSQYFQTVTDYGKDLMEK (7-10, 12), EQLTPLIK (6-9), KAGTELVNFLSYFVELGTQPATQ (6-12, 15, 16, 17, 18, 19, 20, 22, 24), QAKEPCVESLVSQYFQTVTDYGK (7-8), SKEQLTPLIK (6-10, 12), SPELQAEAK (6-10, 12), VKSPELQAEAK (5, 7, 8)
HPP 44	8	23	AGTELVNFLSYFVELGTQPATQ (7-10), EPCVESLVSQYFQTVTDYGK (6-10), EPCVESLVSQYFQTVTDYGKDLMEK (7-8), EQLTPLIK (8), KAGTELVNFLSYFVELGTQPATQ (7-9), QAKEPCVESLVSQYFQTVTDYGK (7-8), SKEQLTPLIK (7-9), SPELQAEAK (7-8), SYFEK (7-8), VKSPELQAEAK (7-9)
HPP 44	8	24	AGTELVNFLSYFVELGTQPATQ (5-8), EPCVESLVSQYFQTVTDYGK (3-8), EQLTPLIK (7), KAGTELVNFLSYFVELGTQPATQ (5-7), SKEQLTPLIK (5-7), VKSPELQAEAK (6-7)
HPP 44	9	16	EPCVESLVSQYFQTVTDYGK (11-12, 15, 16), SPELQAEAK (11)
HPP 44	9	17	AGTELVNFLSYFVELGTQPATQ (1-3, 10, 11, 12, 13, 14, 17, 18, 19), EPCVESLVSQYFQTVTDYGK (1-3, 6, 8, 9, 10, 11, 12, 14, 15, 16, 17, 19, 23), KAGTELVNFLSYFVELGTQPATQ (10-12, 14, 15, 16, 17), QAKEPCVESLVSQYFQTVTDYGK (13), SKEQLTPLIK (10, 12, 13, 14, 15, 16, 17), SPELQAEAK (10, 12), VKSPELQAEAK (9-15, 17, 18)
HPP 44	9	18	EPCVESLVSQYFQTVTDYGK (7-13), EPCVESLVSQYFQTVTDYGKDLMEK (12), KAGTELVNFLSYFVELGTQPATQ (11), QAKEPCVESLVSQYFQTVTDYGK (11), SKEQLTPLIK (9, 11, 12, 13), VKSPELQAEAK (11-12)
HPP 44	9	19	AGTELVNFLSYFVELGTQPATQ (9-14), EPCVESLVSQYFQTVTDYGK (7-17), EQLTPLIK (11), KAGTELVNFLSYFVELGTQPATQ (7-8, 10, 11, 13, 14, 16), SKEQLTPLIK (10-16), SPELQAEAK (10-15), SYFEK (11), VKSPELQAEAK (9-12)
HPP 44	9	20	AGTELVNFLSYFVELGTQPATQ (6-11, 14), EPCVESLVSQYFQTVTDYGK (6-17), EPCVESLVSQYFQTVTDYGKDLMEK (9), EQLTPLIK (8, 11, 12), KAGTELVNFLSYFVELGTQPATQ (6-10, 13), SKEQLTPLIK (6-7, 9, 10, 11), SPELQAEAK (6-8, 10, 11), SYFEK (8), VKSPELQAEAK (9, 11, 13)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	9	21	AGTELVNFLSYFVELGTQPATQ (1, 7, 8, 9, 10, 13, 14, 18, 24), DLMEK (8), EPCVESLVSQYFQTVTDYGK (1, 3, 4, 7, 8, 9, 10, 11, 12, 13, 14, 15, 17, 18, 19, 20, 21, 22, 23, 24), EPCVESLVSQYFQTVTDYGKDLMEK (8-10), EQLTPLIK (7-10), KAGTELVNFLSYFVELGTQPATQ (7, 9, 10, 11, 12, 13, 14, 15), QAKEPCVESLVSQYFQTVTDYGK (9), SKEQLTPLIK (8-10), SPELQAEAK (7-11, 13), SYFEK (7-8), VKSPELQAEAK (7-9, 11)
HPP 44	9	22	AGTELVNFLSYFVELGTQPATQ (7-11), EPCVESLVSQYFQTVTDYGK (6, 8, 9), EPCVESLVSQYFQTVTDYGKDLMEK (7), KAGTELVNFLSYFVELGTQPATQ (7-8, 10), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (6-8), SPELQAEAKSYFEK (7)
HPP 44	9	23	AGTELVNFLSYFVELGTQPATQ (7, 9), EPCVESLVSQYFQTVTDYGK (7-9), EPCVESLVSQYFQTVTDYGKDLMEK (7-8), KAGTELVNFLSYFVELGTQPATQ (7-8), SKEQLTPLIK (7, 9)
HPP 44	9	24	EPCVESLVSQYFQTVTDYGK (7-8), SKEQLTPLIK (7)
HPP 44	10	18	AGTELVNFLSYFVELGTQPATQ (8), EPCVESLVSQYFQTVTDYGK (8), KAGTELVNFLSYFVELGTQPATQ (8), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (8)
HPP 44	10	19	AGTELVNFLSYFVELGTQPATQ (8-13), EPCVESLVSQYFQTVTDYGK (8-12), KAGTELVNFLSYFVELGTQPATQ (8-10), SKEQLTPLIK (9-12), SPELQAEAK (9-10, 12), VKSPELQAEAK (11-12)
HPP 44	10	20	AGTELVNFLSYFVELGTQPATQ (8, 11), EPCVESLVSQYFQTVTDYGK (7-9, 11), KAGTELVNFLSYFVELGTQPATQ (8-10), SKEQLTPLIK (9), VKSPELQAEAK (9)
HPP 44	10	21	AGTELVNFLSYFVELGTQPATQ (8, 10, 11, 14), EPCVESLVSQYFQTVTDYGK (8-14), EPCVESLVSQYFQTVTDYGKDLMEK (8-9, 13), EQLTPLIK (10, 12), KAGTELVNFLSYFVELGTQPATQ (10-12), QAKEPCVESLVSQYFQTVTDYGK (8, 10), SKEQLTPLIK (9-13), SPELQAEAK (9, 12), VKSPELQAEAK (9-11)
HPP 44	10	22	AGTELVNFLSYFVELGTQPATQ (7-9), EPCVESLVSQYFQTVTDYGK (7-10, 12, 13, 15, 16, 23), EQLTPLIK (8-9), KAGTELVNFLSYFVELGTQPATQ (7-9), SKEQLTPLIK (8-9, 12)
HPP 44	10	23	AGTELVNFLSYFVELGTQPATQ (12), EPCVESLVSQYFQTVTDYGK (9-10, 12)
HPP 44	10	26	AGTELVNFLSYFVELGTQPATQ (6)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	10	27	SPELQAEAK (13)
HPP 44	11	8	AGTELVNFLSYFVELGTQPATQ (6, 9, 10, 16, 21), KAGTELVNFLSYFVELGTQPATQ (7, 9, 10, 11, 14, 17)
HPP 44	11	16	AGTELVNFLSYFVELGTQPATQ (9)
HPP 44	11	18	AGTELVNFLSYFVELGTQPATQ (8-12), EPCVESLVSQYFQTVTDYGK (8-12), EQLTPLIK (9, 11), KAGTELVNFLSYFVELGTQPATQ (8-10), QAKEPCVESLVSQYFQTVTDYGK (8, 12), SKEQLTPLIK (9, 11, 12), SPELQAEAK (9)
HPP 44	11	19	AGTELVNFLSYFVELGTQPATQ (9-16), EPCVESLVSQYFQTVTDYGK (8-16), EPCVESLVSQYFQTVTDYGKDLMEK (12-13), EQLTPLIK (10-11, 14), KAGTELVNFLSYFVELGTQPATQ (9-13), QAKEPCVESLVSQYFQTVTDYGK (12), SKEQLTPLIK (9-11, 13, 14, 15, 16), SPELQAEAK (10-11, 13), SYFEK (10, 13), VKSPELQAEAK (10-13, 16)
HPP 44	11	20	AGTELVNFLSYFVELGTQPATQ (11-12), EPCVESLVSQYFQTVTDYGK (8-14), EPCVESLVSQYFQTVTDYGKDLMEK (10-11), EQLTPLIK (10-11, 14), KAGTELVNFLSYFVELGTQPATQ (8-14), SKEQLTPLIK (8-13), VKSPELQAEAK (10)
HPP 44	11	21	AGTELVNFLSYFVELGTQPATQ (13-14), EPCVESLVSQYFQTVTDYGK (7-15), EPCVESLVSQYFQTVTDYGKDLMEK (9, 11), EQLTPLIK (8, 10, 11, 12, 14), KAGTELVNFLSYFVELGTQPATQ (9-13, 15), SKEQLTPLIK (7-14), SPELQAEAK (11), VKSPELQAEAK (8-9, 11, 12)
HPP 44	11	22	AGTELVNFLSYFVELGTQPATQ (5, 7, 8, 9, 11, 12, 15, 18, 21, 22), EPCVESLVSQYFQTVTDYGK (7-13), EQLTPLIK (7), KAGTELVNFLSYFVELGTQPATQ (5, 7, 8, 9, 10), SKEQLTPLIK (7-9, 11, 12, 13), SPELQAEAK (6, 10, 11, 12, 13, 14), SYFEK (7), VKSPELQAEAK (7, 9)
HPP 44	11	23	AGTELVNFLSYFVELGTQPATQ (9-10), EPCVESLVSQYFQTVTDYGK (7-10), EPCVESLVSQYFQTVTDYGKDLMEK (8-9), KAGTELVNFLSYFVELGTQPATQ (8-9), SKEQLTPLIK (8-9)
HPP 44	11	24	EPCVESLVSQYFQTVTDYGK (6-8), EQLTPLIK (7), SKEQLTPLIK (6-7)
HPP 44	11	30	AGTELVNFLSYFVELGTQPATQ (2, 8, 10, 12, 18, 19, 22)
HPP 44	12	13	AGTELVNFLSYFVELGTQPATQ (1, 5, 6, 9, 10, 11, 14)
HPP 44	12	18	AGTELVNFLSYFVELGTQPATQ (7-8), EPCVESLVSQYFQTVTDYGK (7-8), KAGTELVNFLSYFVELGTQPATQ (7-8), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (7-8), VKSPELQAEAK (8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	12	19	AGTELVNFLSYFVELGTQPATQ (14), EPCVESLVSQYFQTVTDYGK (8-10, 13, 14), KAGTELVNFLSYFVELGTQPATQ (9-10), QAKEPCVESLVSQYFQTVTDYGK (10), SPELQAEAK (13)
HPP 44	12	20	AGTELVNFLSYFVELGTQPATQ (7, 11, 12, 13, 15), EPCVESLVSQYFQTVTDYGK (5-11), EPCVESLVSQYFQTVTDYGKDLMEK (8, 11), EQLTPLIK (7-8), KAGTELVNFLSYFVELGTQPATQ (7-9), QAKEPCVESLVSQYFQTVTDYGK (11), SKEQLTPLIK (8-12), SPELQAEAK (8), VKSPELQAEAK (8, 10, 11)
HPP 44	12	21	AGTELVNFLSYFVELGTQPATQ (8-13), EPCVESLVSQYFQTVTDYGK (6-14, 16), EPCVESLVSQYFQTVTDYGKDLMEK (8, 11, 12), EQLTPLIK (7, 9), KAGTELVNFLSYFVELGTQPATQ (8-12), QAKEPCVESLVSQYFQTVTDYGK (11-12), SKEQLTPLIK (8-13), SPELQAEAK (10-11), VKSPELQAEAK (8-13)
HPP 44	12	23	EPCVESLVSQYFQTVTDYGK (9)
HPP 44	12	28	AGTELVNFLSYFVELGTQPATQ (4, 7)
HPP 44	13	12	AGTELVNFLSYFVELGTQPATQ (1, 8, 10, 12, 15, 19, 20), KAGTELVNFLSYFVELGTQPATQ (14)
HPP 44	13	18	AGTELVNFLSYFVELGTQPATQ (8-11), EPCVESLVSQYFQTVTDYGK (8-11), KAGTELVNFLSYFVELGTQPATQ (8-10), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (8-9, 11)
HPP 44	13	19	AGTELVNFLSYFVELGTQPATQ (5, 13, 16, 21, 22), EPCVESLVSQYFQTVTDYGK (8-13, 21), KAGTELVNFLSYFVELGTQPATQ (5-6, 8, 13), QAKEPCVESLVSQYFQTVTDYGK (10), SKEQLTPLIK (8, 10, 11, 12, 13, 16), SPELQAEAK (9), VKSPELQAEAK (9, 13)
HPP 44	13	20	AGTELVNFLSYFVELGTQPATQ (8-10), EPCVESLVSQYFQTVTDYGK (7-11), EQLTPLIK (8), KAGTELVNFLSYFVELGTQPATQ (8-9), SKEQLTPLIK (6-11), VKSPELQAEAK (8-9)
HPP 44	13	21	AGTELVNFLSYFVELGTQPATQ (8-11, 13, 14, 15, 16, 17), EPCVESLVSQYFQTVTDYGK (6-11, 13, 15, 16, 17, 19), EPCVESLVSQYFQTVTDYGKDLMEK (9, 13), EQLTPLIK (8, 10, 11), KAGTELVNFLSYFVELGTQPATQ (8-11, 13, 14, 15, 17), QAKEPCVESLVSQYFQTVTDYGK (9, 13), SKEQLTPLIK (7-11, 13), SPELQAEAK (8, 11, 12), SYFEK (9-10), VKSPELQAEAK (9-11)
HPP 44	13	22	AGTELVNFLSYFVELGTQPATQ (8-12), EPCVESLVSQYFQTVTDYGK (7-11), EQLTPLIK (9), KAGTELVNFLSYFVELGTQPATQ (7-10), SKEQLTPLIK (9), SPELQAEAK (9)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	13	23	AGTELVNFLSYFVELGTQPATQ (8-9, 13, 14), EPCVESLVSQYFQTVTDYGK (7-13), EQLTPLIK (8-10), KAGTELVNFLSYFVELGTQPATQ (8-9), SKEQLTPLIK (8, 10), SPELQAEAK (9), SYFEK (9)
HPP 44	13	25	EPCVESLVSQYFQTVTDYGK (7)
HPP 44	14	14	AGTELVNFLSYFVELGTQPATQ (5, 12, 19)
HPP 44	14	16	AGTELVNFLSYFVELGTQPATQ (14-15), EPCVESLVSQYFQTVTDYGK (1, 14)
HPP 44	14	17	AGTELVNFLSYFVELGTQPATQ (13, 16), EPCVESLVSQYFQTVTDYGK (14, 18, 19), KAGTELVNFLSYFVELGTQPATQ (13, 18), SKEQLTPLIK (14, 16), VKSPELQAEAK (13, 16)
HPP 44	14	18	EPCVESLVSQYFQTVTDYGK (10-11, 13, 14, 15), EPCVESLVSQYFQTVTDYGKDLMEK (14), EQLTPLIK (10), KAGTELVNFLSYFVELGTQPATQ (14), SKEQLTPLIK (10, 13, 14), VKSPELQAEAK (10, 14)
HPP 44	14	19	AGTELVNFLSYFVELGTQPATQ (10, 14, 17), EPCVESLVSQYFQTVTDYGK (10, 14, 16, 17, 18, 19), EPCVESLVSQYFQTVTDYGKDLMEK (17-18), EQLTPLIK (14, 17, 18), KAGTELVNFLSYFVELGTQPATQ (17-18), SKEQLTPLIK (14, 16, 17, 18), VKSPELQAEAK (14, 18)
HPP 44	14	20	AGTELVNFLSYFVELGTQPATQ (8-9, 11, 12, 18), EPCVESLVSQYFQTVTDYGK (8-11, 13, 14), KAGTELVNFLSYFVELGTQPATQ (8-9, 11, 13), SKEQLTPLIK (9-10, 13), SPELQAEAK (8)
HPP 44	14	21	AGTELVNFLSYFVELGTQPATQ (8-10, 13), EPCVESLVSQYFQTVTDYGK (8-14), KAGTELVNFLSYFVELGTQPATQ (8-9)
HPP 44	14	22	AGTELVNFLSYFVELGTQPATQ (9, 12), EPCVESLVSQYFQTVTDYGK (7-12), EQLTPLIK (9), KAGTELVNFLSYFVELGTQPATQ (7-10), SKEQLTPLIK (7, 9, 10), SPELQAEAK (9-10)
HPP 44	14	23	AGTELVNFLSYFVELGTQPATQ (6, 11), EPCVESLVSQYFQTVTDYGK (6-11), EQLTPLIK (7), KAGTELVNFLSYFVELGTQPATQ (7-9), SKEQLTPLIK (7-8, 10)
HPP 44	14	24	AGTELVNFLSYFVELGTQPATQ (7-8), EPCVESLVSQYFQTVTDYGK (5-8), EQLTPLIK (5, 7), KAGTELVNFLSYFVELGTQPATQ (5-7), SKEQLTPLIK (5-6)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	14	25	AGTELVNFLSYFVELGTQPATQ (5-7, 9, 11, 12, 14, 16), EPCVESLVSQYFQTVTDYGK (5-9, 11, 12), EPCVESLVSQYFQTVTDYGKDLMEK (8), KAGTELVNFLSYFVELGTQPATQ (6-8), SKEQLTPLIK (6-7), SPELQAEAK (6-7)
HPP 44	14	26	EPCVESLVSQYFQTVTDYGK (5)
HPP 44	15	2	AGTELVNFLSYFVELGTQPATQ (5, 9, 20)
HPP 44	15	8	AGTELVNFLSYFVELGTQPATQ (10-11, 22), KAGTELVNFLSYFVELGTQPATQ (10-11)
HPP 44	15	17	EPCVESLVSQYFQTVTDYGK (8-9)
HPP 44	15	18	AGTELVNFLSYFVELGTQPATQ (8-9)
HPP 44	15	19	AGTELVNFLSYFVELGTQPATQ (15), EPCVESLVSQYFQTVTDYGK (16), EPCVESLVSQYFQTVTDYGKDLMEK (12)
HPP 44	15	20	AGTELVNFLSYFVELGTQPATQ (8-9), EPCVESLVSQYFQTVTDYGK (8-9)
HPP 44	15	21	AGTELVNFLSYFVELGTQPATQ (8), EPCVESLVSQYFQTVTDYGK (8-9)
HPP 44	15	22	AGTELVNFLSYFVELGTQPATQ (10), EPCVESLVSQYFQTVTDYGK (9-10), KAGTELVNFLSYFVELGTQPATQ (9), SKEQLTPLIK (9)
HPP 44	15	23	AGTELVNFLSYFVELGTQPATQ (1, 3, 4, 8, 9, 10, 12, 15, 18), EPCVESLVSQYFQTVTDYGK (9), KAGTELVNFLSYFVELGTQPATQ (1, 5, 12, 13, 15)
HPP 44	15	24	AGTELVNFLSYFVELGTQPATQ (7-9), EPCVESLVSQYFQTVTDYGK (7-8)
HPP 44	15	26	EPCVESLVSQYFQTVTDYGK (8)
HPP 44	16	17	EPCVESLVSQYFQTVTDYGK (17)
HPP 44	16	20	AGTELVNFLSYFVELGTQPATQ (1, 8, 9, 10), EPCVESLVSQYFQTVTDYGK (7-10), EQLTPLIK (9), SKEQLTPLIK (10)
HPP 44	16	21	EPCVESLVSQYFQTVTDYGK (7, 10), EQLTPLIK (8), KAGTELVNFLSYFVELGTQPATQ (7), SKEQLTPLIK (7-8)
HPP 44	16	22	AGTELVNFLSYFVELGTQPATQ (6-10), EPCVESLVSQYFQTVTDYGK (6-8, 12, 14), EQLTPLIK (6-7), KAGTELVNFLSYFVELGTQPATQ (9), SKEQLTPLIK (7-8), SPELQAEAK (7)
HPP 44	16	23	AGTELVNFLSYFVELGTQPATQ (6-9), EPCVESLVSQYFQTVTDYGK (6-11), EPCVESLVSQYFQTVTDYGKDLMEK (9), EQLTPLIK (7), KAGTELVNFLSYFVELGTQPATQ (7, 9, 10), QAKEPCVESLVSQYFQTVTDYGK (7, 9), SKEQLTPLIK (8), SPELQAEAK (7-9), VKSPELQAEAK (8-9)
HPP 44	16	24	EPCVESLVSQYFQTVTDYGK (6)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	16	25	EPCVESLVSQYFQTVTDYGK (6)
HPP 44	16	29	AGTELVNFLSYFVELGTQPATQ (5-7, 9, 14, 15, 18, 22), EPCVESLVSQYFQTVTDYGK (1, 7, 9, 10, 11, 12, 13, 14, 17, 18, 19, 20, 21, 22, 24)
HPP 44	17	1	AGTELVNFLSYFVELGTQPATQ (2-8, 15, 16, 19), EPCVESLVSQYFQTVTDYGK (1-10, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24), KAGTELVNFLSYFVELGTQPATQ (3, 7, 10, 22)
HPP 44	17	19	AGTELVNFLSYFVELGTQPATQ (9), EPCVESLVSQYFQTVTDYGK (9), KAGTELVNFLSYFVELGTQPATQ (9), SKEQLTPLIK (9), VKSPELQAEAK (9)
HPP 44	17	20	AGTELVNFLSYFVELGTQPATQ (9), EPCVESLVSQYFQTVTDYGK (7-9, 11, 12), EQLTPLIK (10), KAGTELVNFLSYFVELGTQPATQ (7-9), QAKEPCVESLVSQYFQTVTDYGK (7), SKEQLTPLIK (7-10, 12), SPELQAEAK (10)
HPP 44	17	21	AGTELVNFLSYFVELGTQPATQ (8-9, 11, 12, 14), EPCVESLVSQYFQTVTDYGK (7-14), EPCVESLVSQYFQTVTDYGKDLMEK (10-13), EQLTPLIK (9), KAGTELVNFLSYFVELGTQPATQ (8-12), SKEQLTPLIK (9-13), SPELQAEAK (8-11), SYFEK (9), VKSPELQAEAK (9, 11, 12, 13)
HPP 44	17	22	AGTELVNFLSYFVELGTQPATQ (6-10), EPCVESLVSQYFQTVTDYGK (6-9), EPCVESLVSQYFQTVTDYGKDLMEK (8), EQLTPLIK (7), EQLTPLIKK (8), KAGTELVNFLSYFVELGTQPATQ (6-9), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (7-9), SPELQAEAKSYFEK (8)
HPP 44	17	23	AGTELVNFLSYFVELGTQPATQ (7-9), EPCVESLVSQYFQTVTDYGK (6-9), EPCVESLVSQYFQTVTDYGKDLMEK (7), KAGTELVNFLSYFVELGTQPATQ (7-8), SKEQLTPLIK (7-8)
HPP 44	17	24	AGTELVNFLSYFVELGTQPATQ (6, 9), EPCVESLVSQYFQTVTDYGK (5-7), EQLTPLIK (6-7), KAGTELVNFLSYFVELGTQPATQ (6-7), SKEQLTPLIK (5, 7), VKSPELQAEAK (7)
HPP 44	17	25	EPCVESLVSQYFQTVTDYGK (5, 7), VKSPELQAEAK (5)
HPP 44	17	28	EPCVESLVSQYFQTVTDYGK (9)
HPP 44	18	9	AGTELVNFLSYFVELGTQPATQ (2-5, 9, 10, 11, 13, 16, 18, 19, 21), EPCVESLVSQYFQTVTDYGK (1-22), KAGTELVNFLSYFVELGTQPATQ (1, 3, 6, 7, 8, 9, 10, 12, 18, 19, 20, 22)
HPP 44	18	18	AGTELVNFLSYFVELGTQPATQ (8), EPCVESLVSQYFQTVTDYGK (8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 44	18	19	EPCVESLVSQYFQTVTDYGK (9-10), EQLTPLIKK (9), KAGTELVNFLSYFVELGTQPATQ (9), QAKEPCVESLVSQYFQTVTDYGK (9), SKEQLTPLIK (9), SYFEK (10), VKSPELQAEAK (8-10)
HPP 44	18	20	AGTELVNFLSYFVELGTQPATQ (8, 10, 11, 12, 13), EPCVESLVSQYFQTVTDYGK (7-12), EQLTPLIK (7, 9), KAGTELVNFLSYFVELGTQPATQ (7-8), QAKEPCVESLVSQYFQTVTDYGK (7-8), SKEQLTPLIK (7-9), SYFEK (9), VKSPELQAEAK (7-9)
HPP 44	18	21	AGTELVNFLSYFVELGTQPATQ (7, 9, 11, 12), EPCVESLVSQYFQTVTDYGK (7-12), EQLTPLIK (8, 11, 12), KAGTELVNFLSYFVELGTQPATQ (7-12), SKEQLTPLIK (8-12), VKSPELQAEAK (9, 11, 12)
HPP 44	18	22	AGTELVNFLSYFVELGTQPATQ (7-9, 11), EPCVESLVSQYFQTVTDYGK (6-10), EPCVESLVSQYFQTVTDYGKDLMEK (7-8), EQLTPLIK (7-8), KAGTELVNFLSYFVELGTQPATQ (7-9), QAKEPCVESLVSQYFQTVTDYGK (8), SKEQLTPLIK (6-9), VKSPELQAEAK (6)
HPP 44	18	23	EPCVESLVSQYFQTVTDYGK (6-9), EPCVESLVSQYFQTVTDYGKDLMEK (7), EQLTPLIK (7), KAGTELVNFLSYFVELGTQPATQ (7), SKEQLTPLIK (8)
HPP 44	18	24	EPCVESLVSQYFQTVTDYGK (4-6), SKEQLTPLIK (4-5)
HPP 44	18	25	AGTELVNFLSYFVELGTQPATQ (6), EPCVESLVSQYFQTVTDYGK (6), EPCVESLVSQYFQTVTDYGKDLMEK (5), SKEQLTPLIK (5-6)
HPP 44	18	26	AGTELVNFLSYFVELGTQPATQ (6), EPCVESLVSQYFQTVTDYGK (7-8), EQLTPLIK (7), KAGTELVNFLSYFVELGTQPATQ (7), VKSPELQAEAK (6)
HPP 44	18	27	EPCVESLVSQYFQTVTDYGK (7, 10)
HPP 44	18	28	EPCVESLVSQYFQTVTDYGK (6)
HPP 44	18	29	EPCVESLVSQYFQTVTDYGK (9)
HPP 44	18	30	EPCVESLVSQYFQTVTDYGK (9-10)
HPP 45	5	18	ATLVCLISDFYPGAVTLAWK (4), YAASSYLSLTPEQWK (4)
HPP 45	8	15	ATLVCLISDFYPGAVTLAWK (15), LTVLGQPK (15), QSNNKYAASSYLSLTPEQWK (15), YAASSYLSLTPEQWK (15)
HPP 46	7	15	SGTASVVCLLNNFYPR (9), VDNALQSGNSQESVTEQDSK (9)
HPP 46	8	30	VYACEVTHQGLSSPVTK (3)
HPP 46	9	25	VDNALQSGNSQESVTEQDSK (4), VYACEVTHQGLSSPVTK (4)
HPP 47	8	10	VLSNTEDLPLVTK (7)
HPP 47	8	11	VLSNTEDLPLVTK (10)
HPP 47	9	10	VLSNTEDLPLVTK (9, 11)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 47	9	11	VLSNTEDLPLVTK (11)
HPP 48	9	20	KGDTFSCMVGHEALPLAFTQK (7), QKPSQGTTTFAVTSILR (7)
HPP 48	9	22	QKPSQGTTTFAVTSILR (7)
HPP 48	9	23	KGDTFSCMVGHEALPLAFTQK (5), QKPSQGTTTFAVTSILR (5)
HPP 49	2	12	EVPLNTIIFMGR (9)
HPP 49	3	13	ANRPFLVFIR (10)
HPP 49	3	14	EVPLNTIIFMGR (9)
HPP 49	4	13	ANRPFLVFIR (8-10), EVPLNTIIFMGR (8-10), SLNPNRVTFK (8)
HPP 49	4	14	EVPLNTIIFMGR (9)
HPP 49	4	15	EVPLNTIIFMGR (8)
HPP 49	5	13	EVPLNTIIFMGR (9-10)
HPP 49	5	15	EVPLNTIIFMGR (7)
HPP 49	5	17	ANRPFLVFIR (5), FATTFYQHLADSK (5)
HPP 49	5	18	EVPLNTIIFMGR (4)
HPP 49	5	20	EVPLNTIIFMGR (3)
HPP 49	6	11	ANRPFLVFIR (10), EVPLNTIIFMGR (11-12), NDNDNIFLSPLSISTAFAMTK (10-12)
HPP 49	6	12	EVPLNTIIFMGR (8-9)
HPP 49	6	13	ANRPFLVFIR (8-9), EVPLNTIIFMGR (9-11), FATTFYQHLADSK (8-9), NDNDNIFLSPLSISTAFAMTK (8-9)
HPP 49	6	21	EQLQDMGLVDLFSPEK (8-10), EVPLNTIIFMGR (9-10)
HPP 49	6	23	EQLQDMGLVDLFSPEK (7), EVPLNTIIFMGR (7), HGSPVDICTAKPR (6)
HPP 49	7	10	ANRPFLVFIR (10)
HPP 49	8	11	ATEDEGSEQKIPEATNR (9)
HPP 49	8	12	FATTFYQHLADSK (8), NDNDNIFLSPLSISTAFAMTK (7-8)
HPP 49	8	13	ANRPFLVFIR (8), FATTFYQHLADSK (8)
HPP 49	8	14	NDNDNIFLSPLSISTAFAMTK (6-7)
HPP 49	8	15	EVPLNTIIFMGR (6)
HPP 49	9	4	ATEDEGSEQKIPEATNR (12)
HPP 49	9	5	ATEDEGSEQKIPEATNR (17)
HPP 49	9	16	EQLQDMGLVDLFSPEK (15-16), VAEGTQVLELPFK (14)
HPP 49	10	5	HGSPVDICTAKPR (12, 14)
HPP 49	10	6	ATEDEGSEQKIPEATNR (8), HGSPVDICTAKPR (8)
HPP 49	10	13	ATEDEGSEQKIPEATNR (9), FATTFYQHLADSK (9), HGSPVDICTAKPR (8)
HPP 49	10	16	VAEGTQVLELPFK (9)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 49	10	18	VAEGTQVLELPFK (9)
HPP 49	10	22	EQLQDMGLVDLFSPEK (5)
HPP 49	11	7	ATEDEGSEQKIPEATNR (12), HGSPVDICTAKPR (12)
HPP 49	11	14	EVPLNTIIFMGR (7)
HPP 49	11	17	VAEGTQVLELPFK (14)
HPP 49	11	20	VAEGTQVLELPFK (7)
HPP 49	11	23	EQLQDMGLVDLFSPEK (6)
HPP 49	12	14	EVPLNTIIFMGR (7)
HPP 49	13	18	ANRPFLVFIR (8), EQLQDMGLVDLFSPEK (9), EVPLNTIIFMGR (8-9), VAEGTQVLELPFKGDDITMVLILPKPEK (8)
HPP 49	14	17	EQLQDMGLVDLFSPEK (14), FATTFYQHLADSK (15), VAEGTQVLELPFK (14)
HPP 49	14	18	DDLYVSDAFHK (8), EQLQDMGLVDLFSPEK (8-9), EVPLNTIIFMGR (9), FATTFYQHLADSK (9), NDNDNIFLSPLSISTAFAMTK (9), VAEGTQVLELPFK (8-9)
HPP 49	14	19	EQLQDMGLVDLFSPEK (9, 11, 12), EVPLNTIIFMGR (11-12), NDNDNIFLSPLSISTAFAMTK (11-12), TSDQIHFFFAK (9-10), VAEGTQVLELPFK (12)
HPP 49	14	20	ANRPFLVFIR (8), ATEDEGSEQKIPEATNR (7)
HPP 49	14	21	EQLQDMGLVDLFSPEK (7-8), GDDITMVLILPKPEK (8), VAEGTQVLELPFK (8)
HPP 49	14	22	EQLQDMGLVDLFSPEK (6), EVPLNTIIFMGR (6), NDNDNIFLSPLSISTAFAMTK (6-7), TSDQIHFFFAK (6), VAEGTQVLELPFK (6-7)
HPP 49	14	23	ANRPFLVFIR (6), DDLYVSDAFHK (6), GDDITMVLILPKPEK (6), VAEGTQVLELPFK (6)
HPP 49	14	24	EQLQDMGLVDLFSPEK (5), EVPLNTIIFMGR (5), VAEGTQVLELPFK (5)
HPP 49	14	25	DDLYVSDAFHK (4), EVPLNTIIFMGR (5), NDNDNIFLSPLSISTAFAMTK (4), VAEGTQVLELPFK (5)
HPP 49	14	26	EQLQDMGLVDLFSPEK (4-5), VAEGTQVLELPFK (4)
HPP 49	14	27	EQLQDMGLVDLFSPEK (4)
HPP 49	14	28	EQLQDMGLVDLFSPEK (6)
HPP 49	14	30	EQLQDMGLVDLFSPEK (5)
HPP 49	15	13	ANRPFLVFIR (8), EVPLNTIIFMGR (11)
HPP 49	15	15	EVPLNTIIFMGR (9), HGSPVDICTAKPR (21)

Table 3			
Protein	**CEX**	**RP1**	**Tryptic Sequence (RP2 fractions)**
HPP 49	15	16	ADGESCSASMMYQEGK (16), ATEDEGSEQKIPEATNR (14, 16), EQLQDMGLVDLFSPEK (12-17), EVPLNTIIFMGR (14-16), FATTFYQHLADSK (14, 17), HGSPVDICTAKPR (16, 18), IEDGFSLKEQLQDMGLVDLFSPEK (14), NDNDNIFLSPLSISTAFAMTK (12-16), TSDQIHFFFAK (15), VAEGTQVLELPFK (13-14, 17)
HPP 49	15	17	HGSPVDICTAKPR (17)
HPP 49	15	18	ANRPFLVFIR (10-12), DDLYVSDAFHK (10-11), EQLQDMGLVDLFSPEK (9-12), EVPLNTIIFMGR (10-12), FATTFYQHLADSK (10), FRIEDGFSLK (12), NDNDNIFLSPLSISTAFAMTK (9-12), TSDQIHFFFAK (10, 12), VAEGTQVLELPFK (9-12)
HPP 49	15	19	AFLEVNEEGSEAAASTAVVIAGR (11-12), ANRPFLVFIR (12), ATEDEGSEQKIPEATNR (11-12), DDLYVSDAFHK (12), EQLQDMGLVDLFSPEK (11-13), EVPLNTIIFMGR (11, 13), FATTFYQHLADSK (10-13), HGSPVDICTAKPR (11, 14), IEDGFSLK (12), NDNDNIFLSPLSISTAFAMTK (11-13), TSDQIHFFFAK (10-13)
HPP 49	15	20	DDLYVSDAFHK (7), EQLQDMGLVDLFSPEK (7-8), FATTFYQHLADSK (7-8), HGSPVDICTAKPR (7), NDNDNIFLSPLSISTAFAMTK (7), VAEGTQVLELPFK (7-8)
HPP 49	15	21	EQLQDMGLVDLFSPEK (8), FATTFYQHLADSK (7), HGSPVDICTAKPR (8), NDNDNIFLSPLSISTAFAMTK (7)
HPP 49	15	22	EQLQDMGLVDLFSPEK (6), EVPLNTIIFMGR (6)
HPP 49	15	24	EQLQDMGLVDLFSPEK (5), FATTFYQHLADSK (5), NDNDNIFLSPLSISTAFAMTK (4-5), VAEGTQVLELPFK (5)
HPP 49	15	25	EVPLNTIIFMGR (5), NDNDNIFLSPLSISTAFAMTK (5)
HPP 49	15	26	EQLQDMGLVDLFSPEK (4), EVPLNTIIFMGR (4), NDNDNIFLSPLSISTAFAMTK (5), VAEGTQVLELPFK (3-4)
HPP 49	15	27	ATEDEGSEQKIPEATNR (4), FATTFYQHLADSK (4), LPGIVAEGR (4)
HPP 49	16	14	ANRPFLVFIR (9), EVPLNTIIFMGR (7-9)
HPP 49	16	15	EVPLNTIIFMGR (15)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 49	16	17	AFLEVNEEGSEAAASTAVVIAGR (16), ANRPFLVFIR (14-16, 18, 20), ATEDEGSEQKIPEATNR (16, 19, 20), DDLYVSDAFHK (17, 19, 20), EQLQDMGLVDLFSPEK (14-20), EVPLNTIIFMGR (14-21), FATTFYQHLADSK (16-17, 19, 20, 21), FRIEDGFSLK (15), IEDGFSLK (19-21), IEDGFSLKEQLQDMGLVDLFSPEK (16), LPGIVAEGR (19-21), NDNDNIFLSPLSISTAFAMTK (14, 16, 17, 18, 19, 20), TSDQIHFFFAK (15-16, 19, 20, 21), VAEGTQVLELPFK (14-15, 19, 20, 21)
HPP 49	16	18	ATEDEGSEQKIPEATNR (8), EQLQDMGLVDLFSPEK (8, 10), EVPLNTIIFMGR (8-11), FATTFYQHLADSK (9, 11), NDNDNIFLSPLSISTAFAMTK (8, 10), VAEGTQVLELPFK (9-10)
HPP 49	16	19	ANRPFLVFIR (8), ATEDEGSEQKIPEATNR (7), EVPLNTIIFMGR (7-8), HGSPVDICTAKPR (8), TSDQIHFFFAK (8)
HPP 49	16	20	ATEDEGSEQKIPEATNR (7), DDLYVSDAFHK (7), EQLQDMGLVDLFSPEK (7-8), EVPLNTIIFMGR (7-8), FATTFYQHLADSK (8), GDDITMVLILPKPEK (7), IEDGFSLK (7), LPGIVAEGR (7), NDNDNIFLSPLSISTAFAMTK (8), VAEGTQVLELPFK (7, 9)
HPP 49	16	21	AFLEVNEEGSEAAASTAVVIAGR (7-8), ANRPFLVFIR (7-9), DDLYVSDAFHK (7), EQLQDMGLVDLFSPEK (7-8), EVPLNTIIFMGR (6-8), FATTFYQHLADSK (7-8), IEDGFSLK (6), NDNDNIFLSPLSISTAFAMTK (8), TSDQIHFFFAK (7-8), VAEGTQVLELPFK (6-8), VAEGTQVLELPFKGDDITMVLILPKPEK (9)
HPP 49	16	22	ATEDEGSEQKIPEATNR (6), DDLYVSDAFHK (5, 7), EVPLNTIIFMGR (5-6), FATTFYQHLADSK (5, 7), LPGIVAEGR (5), TSDQIHFFFAK (6), VAEGTQVLELPFK (5-6)
HPP 49	16	23	DDLYVSDAFHK (5), EVPLNTIIFMGR (5), FATTFYQHLADSK (5), IEDGFSLK (5), LPGIVAEGR (5), NDNDNIFLSPLSISTAFAMTK (5), VAEGTQVLELPFK (5)
HPP 49	16	24	DDLYVSDAFHK (3-6), EQLQDMGLVDLFSPEK (3-5), EVPLNTIIFMGR (4-5), FATTFYQHLADSK (3-5), GDDITMVLILPKPEK (4), LPGIVAEGR (3), NDNDNIFLSPLSISTAFAMTK (3, 5), TSDQIHFFFAK (4), VAEGTQVLELPFK (3-4)
HPP 49	16	25	EVPLNTIIFMGR (4-6), LPGIVAEGR (3), LQPLDFKENAEQSR (4), TSDQIHFFFAK (4), VAEGTQVLELPFK (4-5)
HPP 49	16	26	DDLYVSDAFHK (5), EQLQDMGLVDLFSPEK (7), EVPLNTIIFMGR (5), FATTFYQHLADSK (5), VAEGTQVLELPFK (5)

Table 3			
Protein	**CEX**	**RP1**	**Tryptic Sequence (RP2 fractions)**
HPP 49	16	27	EVPLNTIIFMGR (5), FATTFYQHLADSK (5), IEDGFSLK (5), VAEGTQVLELPFK (5)
HPP 49	16	28	EQLQDMGLVDLFSPEK (5), EVPLNTIIFMGR (5-7), FATTFYQHLADSK (4-5, 8), LPGIVAEGR (5)
HPP 49	16	29	DDLYVSDAFHK (4-5), EVPLNTIIFMGR (4-6), FATTFYQHLADSK (4-5)
HPP 49	16	30	DDLYVSDAFHK (4-5), EQLQDMGLVDLFSPEK (4-5), EVPLNTIIFMGR (4, 6), FATTFYQHLADSK (5), LQPLDFK (5), NDNDNIFLSPLSISTAFAMTK (4-5)
HPP 49	17	4	HGSPVDICTAKPR (8)
HPP 49	17	6	DIPMNPMCIYR (7), HGSPVDICTAKPR (7-8)
HPP 49	17	7	HGSPVDICTAKPR (8)
HPP 49	17	15	EVPLNTIIFMGR (7)
HPP 49	17	16	EVPLNTIIFMGR (5-7)
HPP 49	17	18	ADGESCSASMMYQEGK (8-9), AFLEVNEEGSEAAASTAVVIAGR (8), ATEDEGSEQKIPEATNR (9), DDLYVSDAFHK (8), EQLQDMGLVDLFSPEK (8-9), EVPLNTIIFMGR (8-9), FATTFYQHLADSK (7-9), GDDITMVLILPKPEK (9), HGSPVDICTAKPR (12), NDNDNIFLSPLSISTAFAMTK (7-9), TSDQIHFFFAK (8), VAEGTQVLELPFK (7-9)
HPP 49	17	19	ATEDEGSEQKIPEATNR (8), EQLQDMGLVDLFSPEK (8-9), EVPLNTIIFMGR (8), FATTFYQHLADSK (8-9), TSDQIHFFFAK (8-9), VAEGTQVLELPFK (8)
HPP 49	17	20	AFLEVNEEGSEAAASTAVVIAGR (7), DDLYVSDAFHK (7, 9, 10), ELFYK (7), EVPLNTIIFMGR (7, 10), FATTFYQHLADSK (7-9), FDTISEK (7), GDDITMVLILPKPEK (9), HGSPVDICTAKPR (9), IEDGFSLK (9), LPGIVAEGR (7-8, 10, 11), TSDQIHFFFAK (7-8), VAEGTQVLELPFK (7-11)
HPP 49	17	21	AFLEVNEEGSEAAASTAVVIAGR (7), ANRPFLVFIR (7), ATEDEGSEQKIPEATNR (7), DDLYVSDAFHK (8), DIPMNPMCIYR (7), EQLQDMGLVDLFSPEK (7-9), EVPLNTIIFMGR (7, 9), FATTFYQHLADSK (7-8), GDDITMVLILPKPEK (7), IEDGFSLK (7), NDNDNIFLSPLSISTAFAMTK (7-9), TSDQIHFFFAK (7), VAEGTQVLELPFK (7-8)
HPP 49	17	22	ANRPFLVFIR (5-6), EQLQDMGLVDLFSPEK (5-6), EVPLNTIIFMGR (5-6), FATTFYQHLADSK (5), IEDGFSLK (5), LPGIVAEGR (5), NDNDNIFLSPLSISTAFAMTK (5-6), TSDQIHFFFAK (5), VAEGTQVLELPFK (5-6)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 49	17	23	AFLEVNEEGSEAAASTAVVIAGR (5), ATEDEGSEQKIPEATNR (6), EQLQDMGLVDLFSPEK (5-6), EVPLNTIIFMGR (5), FATTFYQHLADSK (5-6), FDTISEK (5), IEDGFSLK (5), LPGIVAEGR (6), NDNDNIFLSPLSISTAFAMTK (5-6), VAEGTQVLELPFK (5-6)
HPP 49	17	24	AFLEVNEEGSEAAASTAVVIAGR (4), ANRPFLVFIR (4-5), ATEDEGSEQKIPEATNR (4), DDLYVSDAFHK (4), EQLQDMGLVDLFSPEK (4), EVPLNTIIFMGR (3-5), FATTFYQHLADSK (4-5), IEDGFSLK (4), LPGIVAEGR (3-4), NDNDNIFLSPLSISTAFAMTK (4-6), TSDQIHFFFAK (4), VAEGTQVLELPFK (4)
HPP 49	17	25	AFLEVNEEGSEAAASTAVVIAGR (4), ANRPFLVFIR (4), ATEDEGSEQKIPEATNR (4-5), DDLYVSDAFHK (4), EQLQDMGLVDLFSPEK (3-5), EVPLNTIIFMGR (4-5), FATTFYQHLADSK (3-5), GDDITMVLILPKPEK (4), IEDGFSLK (4), LPGIVAEGR (4), NDNDNIFLSPLSISTAFAMTK (4-5), RVWELSK (4), TSDQIHFFFAK (4), VAEGTQVLELPFK (3-5), VAEGTQVLELPFKGDDITMVLILPKPEK (4)
HPP 49	17	26	AFLEVNEEGSEAAASTAVVIAGR (5), ATEDEGSEQKIPEATNR (5), DDLYVSDAFHK (5), EQLQDMGLVDLFSPEK (3-5, 8), EVPLNTIIFMGR (4), FATTFYQHLADSK (3-5), GDDITMVLILPKPEK (4-5), LPGIVAEGR (5), NDNDNIFLSPLSISTAFAMTK (5), TSDQIHFFFAK (4), VAEGTQVLELPFK (4-5, 8)
HPP 49	17	27	ANRPFLVFIR (5), ATEDEGSEQKIPEATNR (6), DDLYVSDAFHK (5), EQLQDMGLVDLFSPEK (4-7), EVPLNTIIFMGR (5-7), FATTFYQHLADSK (5-7), GDDITMVLILPKPEK (4), IEDGFSLK (5), LPGIVAEGR (5), NDNDNIFLSPLSISTAFAMTK (5-6), VAEGTQVLELPFK (5-6)
HPP 49	17	28	ATEDEGSEQKIPEATNR (6), DDLYVSDAFHK (5, 8), EQLQDMGLVDLFSPEK (4-6), EVPLNTIIFMGR (4-7), FATTFYQHLADSK (5-6), GDDITMVLILPKPEK (5), HGSPVDICTAKPR (5), IEDGFSLK (5), LPGIVAEGR (5), NDNDNIFLSPLSISTAFAMTK (5-7), TSDQIHFFFAK (5), VAEGTQVLELPFK (4-6)
HPP 49	17	29	ADGESCSASMMYQEGK (5), ATEDEGSEQKIPEATNR (5), EQLQDMGLVDLFSPEK (5-6, 8), EVPLNTIIFMGR (5-7), FATTFYQHLADSK (5, 7), IEDGFSLK (5), LPGIVAEGR (5), NDNDNIFLSPLSISTAFAMTK (5-6), TSDQIHFFFAK (5), VAEGTQVLELPFK (5-6)
HPP 49	17	30	ATEDEGSEQKIPEATNR (5-6), EQLQDMGLVDLFSPEK (5-6), EVPLNTIIFMGR (5-6), FATTFYQHLADSK (5-6), NDNDNIFLSPLSISTAFAMTK (5-6)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 49	18	13	ANRPFLVFIR (8)
HPP 49	18	18	ANRPFLVFIR (9), EQLQDMGLVDLFSPEK (8), EVPLNTIIFMGR (8-9), IEDGFSLK (8-9), NDNDNIFLSPLSISTAFAMTK (9), TSDQIHFFFAK (8-9), VAEGTQVLELPFK (8-9)
HPP 49	18	19	DDLYVSDAFHK (9), EQLQDMGLVDLFSPEK (9-11), EVPLNTIIFMGR (8-10), FATTFYQHLADSK (9), GDDITMVLILPKPEK (9), NDNDNIFLSPLSISTAFAMTK (9), TSDQIHFFFAK (9), VAEGTQVLELPFK (8-9)
HPP 49	18	20	ATEDEGSEQKIPEATNR (7), EQLQDMGLVDLFSPEK (7), EVPLNTIIFMGR (7), FATTFYQHLADSK (7), GDDITMVLILPKPEK (7), HGSPVDICTAKPR (7), TSDQIHFFFAK (7)
HPP 49	18	21	ATEDEGSEQKIPEATNR (7), EQLQDMGLVDLFSPEK (7), EVPLNTIIFMGR (7), FATTFYQHLADSK (7), IEDGFSLK (7), NDNDNIFLSPLSISTAFAMTK (7), VAEGTQVLELPFK (7)
HPP 49	18	22	ANRPFLVFIR (6), EQLQDMGLVDLFSPEK (5), EVPLNTIIFMGR (5), NDNDNIFLSPLSISTAFAMTK (6), TSDQIHFFFAK (6), VAEGTQVLELPFK (5-6)
HPP 49	18	23	EQLQDMGLVDLFSPEK (5-6), EVPLNTIIFMGR (5-6), FATTFYQHLADSK (6), TSDQIHFFFAK (6), VAEGTQVLELPFK (5-6)
HPP 49	18	24	EQLQDMGLVDLFSPEK (4), EVPLNTIIFMGR (4), FATTFYQHLADSK (4), IEDGFSLK (4), NDNDNIFLSPLSISTAFAMTK (4), VAEGTQVLELPFK (3)
HPP 49	18	25	ANRPFLVFIR (4), EQLQDMGLVDLFSPEK (4), EVPLNTIIFMGR (4), GDDITMVLILPKPEK (4), HGSPVDICTAKPR (4), NDNDNIFLSPLSISTAFAMTK (4), TSDQIHFFFAK (4), VAEGTQVLELPFK (4)
HPP 49	18	26	ANRPFLVFIR (5), ATEDEGSEQKIPEATNR (5), DDLYVSDAFHK (5), EQLQDMGLVDLFSPEK (5), EVPLNTIIFMGR (5), FATTFYQHLADSK (5), NDNDNIFLSPLSISTAFAMTK (5-6), VAEGTQVLELPFK (4-5)
HPP 49	18	27	AFLEVNEEGSEAAASTAVVIAGR (5), EQLQDMGLVDLFSPEK (5), FATTFYQHLADSK (5), RVWELSK (5), TSDQIHFFFAK (5)
HPP 49	18	28	ANRPFLVFIR (5), EQLQDMGLVDLFSPEK (5), EVPLNTIIFMGR (5), FATTFYQHLADSK (5), GDDITMVLILPKPEK (5), IEDGFSLK (5), NDNDNIFLSPLSISTAFAMTK (5), TSDQIHFFFAK (5), VAEGTQVLELPFK (5)
HPP 49	18	29	ANRPFLVFIR (5), EQLQDMGLVDLFSPEK (4), EVPLNTIIFMGR (4-5), NDNDNIFLSPLSISTAFAMTK (5), TSDQIHFFFAK (5)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 49	18	30	ANRPFLVFIR (5), ATEDEGSEQKIPEATNR (5), EQLQDMGLVDLFSPEK (5), EVPLNTIIFMGR (5), HGSPVDICTAKPR (5)
HPP 50	1	7	GPTGTGESKCPLMVK (8), RYTIAALLSPYSYSTTAVVTNPK (19, 21), YTIAALLSPYSYSTTAVVTNPK (19, 21), YTIAALLSPYSYSTTAVVTNPKE (19, 21)
HPP 50	1	8	YTIAALLSPYSYSTTAVVTNPK (11-13), YTIAALLSPYSYSTTAVVTNPKE (11-13)
HPP 50	1	9	RYTIAALLSPYSYSTTAVVTNPK (12)
HPP 50	1	10	ALGISPFHEHAEVVFTANDSGPR (11), RYTIAALLSPYSYSTTAVVTNPK (8, 11), YTIAALLSPYSYSTTAVVTNPKE (8)
HPP 50	1	11	AADDTWEPFASGK (20), GPTGTGESKCPLMVK (8), GSPAINVAVHVFR (15-16, 18, 19), YTIAALLSPYSYSTTAVVTNPKE (8-9)
HPP 50	1	12	AADDTWEPFASGK (12-14), GSPAINVAVHVFR (15)
HPP 50	1	13	AADDTWEPFASGK (19), ALGISPFHEHAEVVFTANDSGPR (16-17), RYTIAALLSPYSYSTTAVVTNPK (21), TSESGELHGLTTEEEFVEGIYK (17), YTIAALLSPYSYSTTAVVTNPK (19, 21)
HPP 50	1	15	AADDTWEPFASGK (8), GSPAINVAVHVFR (8-9), TSESGELHGLTTEEEFVEGIYK (18)
HPP 50	1	16	ALGISPFHEHAEVVFTANDSGPR (7), RYTIAALLSPYSYSTTAVVTNPK (8), TSESGELHGLTTEEEFVEGIYK (7), YTIAALLSPYSYSTTAVVTNPK (7)
HPP 50	1	19	TSESGELHGLTTEEEFVEGIYK (7), YTIAALLSPYSYSTTAVVTNPK (7)
HPP 50	1	22	TSESGELHGLTTEEEFVEGIYK (4)
HPP 50	1	24	TSESGELHGLTTEEEFVEGIYK (3)
HPP 50	2	7	AADDTWEPFASGK (21), RYTIAALLSPYSYSTTAVVTNPK (16), YTIAALLSPYSYSTTAVVTNPK (16, 19, 20, 21, 23), YTIAALLSPYSYSTTAVVTNPKE (19-21)
HPP 50	2	8	AADDTWEPFASGK (15), RYTIAALLSPYSYSTTAVVTNPK (9-10, 12, 15, 16), YTIAALLSPYSYSTTAVVTNPK (9-10, 12, 13, 14, 15, 17), YTIAALLSPYSYSTTAVVTNPKE (9-11, 13, 15, 16)
HPP 50	2	9	AADDTWEPFASGK (18, 20, 21), GSPAINVAVHVFR (18-22), RYTIAALLSPYSYSTTAVVTNPK (12-13), YTIAALLSPYSYSTTAVVTNPK (15-16), YTIAALLSPYSYSTTAVVTNPKE (9, 12, 13, 15, 16, 17)
HPP 50	2	10	AADDTWEPFASGK (12-16), GSPAINVAVHVFR (12-15, 18), KAADDTWEPFASGK (14), RYTIAALLSPYSYSTTAVVTNPK (9), YTIAALLSPYSYSTTAVVTNPK (9), YTIAALLSPYSYSTTAVVTNPKE (9-10)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	2	11	AADDTWEPFASGK (10), GSPAINVAVHVFR (9-10, 12, 15), YTIAALLSPYSYSTTAVVTNPKE (16, 24)
HPP 50	2	12	AADDTWEPFASGK (20), GSPAINVAVHVFR (8), YTIAALLSPYSYSTTAVVTNPK (17-18)
HPP 50	2	13	AADDTWEPFASGK (17, 23, 24), ALGISPFHEHAEVVFTANDSGPR (16-18), RYTIAALLSPYSYSTTAVVTNPK (17), TSESGELHGLTTEEEFVEGIYK (17-18), YTIAALLSPYSYSTTAVVTNPK (12, 17)
HPP 50	2	14	AADDTWEPFASGK (10, 20), TSESGELHGLTTEEEFVEGIYK (10, 20), YTIAALLSPYSYSTTAVVTNPK (10)
HPP 50	2	15	AADDTWEPFASGK (11-13, 15, 18, 20), GSPAINVAVHVFR (12), RYTIAALLSPYSYSTTAVVTNPK (12), TSESGELHGLTTEEEFVEGIYK (11-12, 14, 16, 17, 18, 20), YTIAALLSPYSYSTTAVVTNPK (13, 17)
HPP 50	2	16	AADDTWEPFASGK (8-9, 14), TSESGELHGLTTEEEFVEGIYK (12, 20)
HPP 50	2	18	GSPAINVAVHVFR (6), TSESGELHGLTTEEEFVEGIYK (6, 8)
HPP 50	2	19	GSPAINVAVHVFR (8)
HPP 50	2	20	AADDTWEPFASGK (7), TSESGELHGLTTEEEFVEGIYK (7)
HPP 50	2	21	TSESGELHGLTTEEEFVEGIYK (7, 10)
HPP 50	2	22	AADDTWEPFASGK (7), ALGISPFHEHAEVVFTANDSGPR (3-4, 6, 9), GSPAINVAVHVFR (3, 6), TSESGELHGLTTEEEFVEGIYK (3-4, 6, 7, 8, 9)
HPP 50	2	23	TSESGELHGLTTEEEFVEGIYK (4-5), YTIAALLSPYSYSTTAVVTNPK (4)
HPP 50	2	25	TSESGELHGLTTEEEFVEGIYK (3)
HPP 50	3	9	GSPAINVAVHVFR (10-13), GSPAINVAVHVFRK (13), YTIAALLSPYSYSTTAVVTNPKE (13)
HPP 50	3	10	ALGISPFHEHAEVVFTANDSGPR (9-11), YTIAALLSPYSYSTTAVVTNPK (9-10), YTIAALLSPYSYSTTAVVTNPKE (10-11)
HPP 50	3	11	AADDTWEPFASGK (10-14), ALGISPFHEHAEVVFTANDSGPR (11-14), GSPAINVAVHVFR (10-13), KAADDTWEPFASGK (10-12), RYTIAALLSPYSYSTTAVVTNPK (13), YTIAALLSPYSYSTTAVVTNPK (12, 14)
HPP 50	3	12	AADDTWEPFASGK (7), ALGISPFHEHAEVVFTANDSGPR (8), ALGISPFHEHAEVVFTANDSGPRR (8), GSPAINVAVHVFR (7-10), GSPAINVAVHVFRK (8), KAADDTWEPFASGK (8), YTIAALLSPYSYSTTAVVTNPK (7-8), YTIAALLSPYSYSTTAVVTNPKE (8)
HPP 50	3	13	AADDTWEPFASGK (8, 12, 13), ALGISPFHEHAEVVFTANDSGPR (8-9), GSPAINVAVHVFR (8-11, 13), YTIAALLSPYSYSTTAVVTNPK (9, 12, 13, 14)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	3	14	ALGISPFHEHAEVVFTANDSGPR (7), TSESGELHGLTTEEEFVEGIYK (10), VEIDTKSYWK (8), YTIAALLSPYSYSTTAVVTNPK (8)
HPP 50	3	15	AADDTWEPFASGK (10), ALGISPFHEHAEVVFTANDSGPR (9), TSESGELHGLTTEEEFVEGIYK (9-12), YTIAALLSPYSYSTTAVVTNPK (9)
HPP 50	3	16	AADDTWEPFASGK (8-9), ALGISPFHEHAEVVFTANDSGPR (8-10), ALGISPFHEHAEVVFTANDSGPRR (8), GSPAINVAVHVFR (8-9), KAADDTWEPFASGK (8-9), TSESGELHGLTTEEEFVEGIYK (8-9), VEIDTKSYWK (8), YTIAALLSPYSYSTTAVVTNPK (8-9), YTIAALLSPYSYSTTAVVTNPKE (9)
HPP 50	3	17	AADDTWEPFASGK (8-11, 14), ALGISPFHEHAEVVFTANDSGPR (7-11), ALGISPFHEHAEVVFTANDSGPRR (9), GSPAINVAVHVFR (8-12), GSPAINVAVHVFRK (9), KAADDTWEPFASGK (8-11), RYTIAALLSPYSYSTTAVVTNPK (8, 10), TSESGELHGLTTEEEFVEGIYK (7-12), YTIAALLSPYSYSTTAVVTNPK (8-11), YTIAALLSPYSYSTTAVVTNPKE (8-10)
HPP 50	3	18	AADDTWEPFASGK (6-8), ALGISPFHEHAEVVFTANDSGPR (7), CPLMVKVLDAVR (7), GSPAINVAVHVFR (8), GSPAINVAVHVFRK (8), KAADDTWEPFASGK (8), RYTIAALLSPYSYSTTAVVTNPK (7), TSESGELHGLTTEEEFVEGIYK (6-7, 9), VLDAVR (7-8), YTIAALLSPYSYSTTAVVTNPK (6-7), YTIAALLSPYSYSTTAVVTNPKE (6)
HPP 50	3	19	AADDTWEPFASGK (7-8), ALGISPFHEHAEVVFTANDSGPR (7-10), KAADDTWEPFASGK (8), TSESGELHGLTTEEEFVEGIYK (7-9), YTIAALLSPYSYSTTAVVTNPK (7-8)
HPP 50	3	20	AADDTWEPFASGK (5-6, 8), ALGISPFHEHAEVVFTANDSGPR (6), GSPAINVAVHVFR (5-6), GSPAINVAVHVFRK (7), KAADDTWEPFASGK (7), TSESGELHGLTTEEEFVEGIYK (5, 7, 8), YTIAALLSPYSYSTTAVVTNPK (5-6), YTIAALLSPYSYSTTAVVTNPKE (7)
HPP 50	3	21	AADDTWEPFASGK (6, 8), ALGISPFHEHAEVVFTANDSGPR (6-7), GSPAINVAVHVFR (7), TSESGELHGLTTEEEFVEGIYK (6, 8), YTIAALLSPYSYSTTAVVTNPKE (7)
HPP 50	3	22	AADDTWEPFASGK (4-5), ALGISPFHEHAEVVFTANDSGPR (5), TSESGELHGLTTEEEFVEGIYK (5), YTIAALLSPYSYSTTAVVTNPK (4-5)
HPP 50	3	23	AADDTWEPFASGK (4-5), ALGISPFHEHAEVVFTANDSGPR (7), GSPAINVAVHVFRK (5), KAADDTWEPFASGK (5), TSESGELHGLTTEEEFVEGIYK (3, 7, 9), YTIAALLSPYSYSTTAVVTNPK (3, 9), YTIAALLSPYSYSTTAVVTNPKE (3-6, 8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	3	24	AADDTWEPFASGK (3-4), ALGISPFHEHAEVVFTANDSGPR (2), GSPAINVAVHVFR (2-4), TSESGELHGLTTEEEFVEGIYK (2), YTIAALLSPYSYSTTAVVTNPK (2)
HPP 50	3	25	AADDTWEPFASGK (3), GSPAINVAVHVFR (4), TSESGELHGLTTEEEFVEGIYK (4), YTIAALLSPYSYSTTAVVTNPK (2)
HPP 50	3	27	ALGISPFHEHAEVVFTANDSGPR (3), TSESGELHGLTTEEEFVEGIYK (2)
HPP 50	3	28	ALGISPFHEHAEVVFTANDSGPR (3)
HPP 50	4	9	GSPAINVAVHVFR (10-11), YTIAALLSPYSYSTTAVVTNPKE (11-13)
HPP 50	4	10	RYTIAALLSPYSYSTTAVVTNPK (9)
HPP 50	4	11	AADDTWEPFASGK (11-12), ALGISPFHEHAEVVFTANDSGPR (11-13), GSPAINVAVHVFR (10, 12), RYTIAALLSPYSYSTTAVVTNPK (13), YTIAALLSPYSYSTTAVVTNPK (9, 11, 12, 13), YTIAALLSPYSYSTTAVVTNPKE (11-12)
HPP 50	4	12	AADDTWEPFASGK (8), ALGISPFHEHAEVVFTANDSGPR (7, 9), ALGISPFHEHAEVVFTANDSGPRR (7), GSPAINVAVHVFR (8-9), GSPAINVAVHVFRK (7-8), VLDAVRGSPAINVAVHVFR (7), YTIAALLSPYSYSTTAVVTNPK (8), YTIAALLSPYSYSTTAVVTNPKE (8)
HPP 50	4	13	AADDTWEPFASGK (8, 11), ALGISPFHEHAEVVFTANDSGPRR (8), GSPAINVAVHVFR (8, 11), YTIAALLSPYSYSTTAVVTNPK (8-9, 11), YTIAALLSPYSYSTTAVVTNPKE (8)
HPP 50	4	14	TSESGELHGLTTEEEFVEGIYK (8)
HPP 50	4	15	AADDTWEPFASGK (9-12, 14), ALGISPFHEHAEVVFTANDSGPR (9, 11, 12, 13), GSPAINVAVHVFR (9-10), KAADDTWEPFASGK (9-10), RYTIAALLSPYSYSTTAVVTNPK (9, 11, 12), TSESGELHGLTTEEEFVEGIYK (9-15), YTIAALLSPYSYSTTAVVTNPK (10-12), YTIAALLSPYSYSTTAVVTNPKE (10-13)
HPP 50	4	16	AADDTWEPFASGK (7, 9, 10, 11, 12, 13), ALGISPFHEHAEVVFTANDSGPR (7-12), ALGISPFHEHAEVVFTANDSGPRR (8), GSPAINVAVHVFR (8-9), GSPAINVAVHVFRK (9), KAADDTWEPFASGK (9-11), TSESGELHGLTTEEEFVEGIYK (7-13), TSESGELHGLTTEEEFVEGIYKVEIDTK (8), YTIAALLSPYSYSTTAVVTNPK (10, 12), YTIAALLSPYSYSTTAVVTNPKE (8-10, 12)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	4	17	AADDTWEPFASGK (8-13, 15), ALGISPFHEHAEVVFTANDSGPR (7-13, 16), ALGISPFHEHAEVVFTANDSGPRR (8-9), CPLMVKVLDAVR (12), GSPAINVAVHVFR (7-12, 16), GSPAINVAVHVFRK (8-10), KAADDTWEPFASGK (8-10, 12, 14), RYTIAALLSPYSYSTTAVVTNPK (11, 14), TSESGELHGLTTEEEFVEGIYK (8-17), TSESGELHGLTTEEEFVEGIYKVEIDTK (8-10), YTIAALLSPYSYSTTAVVTNPK (8-13), YTIAALLSPYSYSTTAVVTNPKE (8-13, 16)
HPP 50	4	18	AADDTWEPFASGK (7-10), ALGISPFHEHAEVVFTANDSGPR (7-10), CPLMVK (7), GSPAINVAVHVFR (6, 8), GSPAINVAVHVFRK (7), KAADDTWEPFASGK (7-9), TSESGELHGLTTEEEFVEGIYK (6-10, 12), TSESGELHGLTTEEEFVEGIYKVEIDTK (9), YTIAALLSPYSYSTTAVVTNPK (6, 8, 9), YTIAALLSPYSYSTTAVVTNPKE (7)
HPP 50	4	19	AADDTWEPFASGK (7-8), ALGISPFHEHAEVVFTANDSGPR (7-9), GSPAINVAVHVFR (7-9), KAADDTWEPFASGK (8), RYTIAALLSPYSYSTTAVVTNPK (7), TSESGELHGLTTEEEFVEGIYK (7-10), YTIAALLSPYSYSTTAVVTNPK (7-9)
HPP 50	4	20	AADDTWEPFASGK (5-8), ALGISPFHEHAEVVFTANDSGPR (5, 7, 8), GSPAINVAVHVFR (5-8), KAADDTWEPFASGK (7), RYTIAALLSPYSYSTTAVVTNPK (7), TSESGELHGLTTEEEFVEGIYK (5-9), YTIAALLSPYSYSTTAVVTNPK (5-8), YTIAALLSPYSYSTTAVVTNPKE (7)
HPP 50	4	22	GSPAINVAVHVFR (4), TSESGELHGLTTEEEFVEGIYK (5, 7, 8), YTIAALLSPYSYSTTAVVTNPK (5)
HPP 50	4	23	AADDTWEPFASGK (3-7), ALGISPFHEHAEVVFTANDSGPR (3, 7), ALGISPFHEHAEVVFTANDSGPRR (5), GSPAINVAVHVFR (3-6, 8), GSPAINVAVHVFRK (5), KAADDTWEPFASGK (4-5), RYTIAALLSPYSYSTTAVVTNPK (3), TSESGELHGLTTEEEFVEGIYK (3-10, 12), YTIAALLSPYSYSTTAVVTNPK (3, 7), YTIAALLSPYSYSTTAVVTNPKE (3, 5)
HPP 50	4	24	AADDTWEPFASGK (2-3), ALGISPFHEHAEVVFTANDSGPR (2), TSESGELHGLTTEEEFVEGIYK (3-4, 7), YTIAALLSPYSYSTTAVVTNPK (2-3), YTIAALLSPYSYSTTAVVTNPKE (2)
HPP 50	4	25	AADDTWEPFASGK (2-3), ALGISPFHEHAEVVFTANDSGPR (2), GSPAINVAVHVFR (2-3), RYTIAALLSPYSYSTTAVVTNPK (2), TSESGELHGLTTEEEFVEGIYK (2-3), YTIAALLSPYSYSTTAVVTNPK (2)
HPP 50	4	26	TSESGELHGLTTEEEFVEGIYK (2-3)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	4	27	TSESGELHGLTTEEEFVEGIYK (2)
HPP 50	5	9	CPLMVK (7), RYTIAALLSPYSYSTTAVVTNPK (11), YTIAALLSPYSYSTTAVVTNPKE (11)
HPP 50	5	10	GSPAINVAVHVFR (9), RYTIAALLSPYSYSTTAVVTNPK (8), YTIAALLSPYSYSTTAVVTNPK (8-9)
HPP 50	5	11	ALGISPFHEHAEVVFTANDSGPR (11-12), GSPAINVAVHVFR (9-10), RYTIAALLSPYSYSTTAVVTNPK (10-11), YTIAALLSPYSYSTTAVVTNPK (9-10), YTIAALLSPYSYSTTAVVTNPKE (9-12)
HPP 50	5	12	AADDTWEPFASGK (7-8), ALGISPFHEHAEVVFTANDSGPR (7), GSPAINVAVHVFR (7-8), KAADDTWEPFASGK (7), RYTIAALLSPYSYSTTAVVTNPK (7), VLDAVR (7), YTIAALLSPYSYSTTAVVTNPK (7-8)
HPP 50	5	13	AADDTWEPFASGK (9), GSPAINVAVHVFR (7, 9), RYTIAALLSPYSYSTTAVVTNPK (8), TSESGELHGLTTEEEFVEGIYK (11), YTIAALLSPYSYSTTAVVTNPK (7, 10)
HPP 50	5	14	AADDTWEPFASGK (7-8), GPTGTGESKCPLMVK (4), GSPAINVAVHVFR (4), TSESGELHGLTTEEEFVEGIYK (7-9), VLDAVRGSPAINVAVHVFR (4-5), YTIAALLSPYSYSTTAVVTNPK (8-9), YTIAALLSPYSYSTTAVVTNPKE (9)
HPP 50	5	15	AADDTWEPFASGK (9-12), ALGISPFHEHAEVVFTANDSGPR (9-12), GSPAINVAVHVFR (9-11, 13), GSPAINVAVHVFRK (10-12), KAADDTWEPFASGK (10-11), TSESGELHGLTTEEEFVEGIYK (8, 10, 11, 12, 13, 17), YTIAALLSPYSYSTTAVVTNPK (6, 9, 10, 11, 12, 13), YTIAALLSPYSYSTTAVVTNPKE (9)
HPP 50	5	16	AADDTWEPFASGK (4, 7, 9, 10, 11, 13, 14, 15), ALGISPFHEHAEVVFTANDSGPR (4, 8, 10, 11, 12, 13, 14, 16), CPLMVKVLDAVR (11-12), GSPAINVAVHVFR (3, 10, 11, 14, 16), KAADDTWEPFASGK (11-12), RYTIAALLSPYSYSTTAVVTNPK (3-4, 10, 14), TSESGELHGLTTEEEFVEGIYK (7-14, 16, 17), YTIAALLSPYSYSTTAVVTNPK (3-4, 8, 9, 10, 11, 12, 13, 14, 17), YTIAALLSPYSYSTTAVVTNPKE (10-11, 15)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	5	17	AADDTWEPFASGK (4, 8, 9, 10, 11, 12, 13, 14, 15), ALGISPFHEHAEVVFTANDSGPR (5, 8, 9, 10, 11, 12, 13, 14), CPLMVKVLDAVR (10-12), GPTGTGESKCPLMVK (10), GSPAINVAVHVFR (4-5, 8, 9, 10, 11, 12, 14), GSPAINVAVHVFRK (9), KAADDTWEPFASGK (8-13), RYTIAALLSPYSYSTTAVVTNPK (4, 11, 12), TSESGELHGLTTEEEFVEGIYK (8-15), TSESGELHGLTTEEEFVEGIYKVEIDTK (8), YTIAALLSPYSYSTTAVVTNPK (3-5, 8, 9, 10, 11, 12, 14), YTIAALLSPYSYSTTAVVTNPKE (4, 8, 10, 11)
HPP 50	5	18	AADDTWEPFASGK (6, 8, 9), ALGISPFHEHAEVVFTANDSGPR (6-8), GSPAINVAVHVFR (6-9), RYTIAALLSPYSYSTTAVVTNPK (6, 9), TSESGELHGLTTEEEFVEGIYK (4-9), VLDAVR (7), YTIAALLSPYSYSTTAVVTNPK (6-8), YTIAALLSPYSYSTTAVVTNPKE (9)
HPP 50	5	19	AADDTWEPFASGK (5-8), ALGISPFHEHAEVVFTANDSGPR (6-7), GSPAINVAVHVFR (5-7), TSESGELHGLTTEEEFVEGIYK (5-9), YTIAALLSPYSYSTTAVVTNPK (5-6, 8), YTIAALLSPYSYSTTAVVTNPKE (5)
HPP 50	5	20	AADDTWEPFASGK (4-8), ALGISPFHEHAEVVFTANDSGPR (3-7), CPLMVK (6), GSPAINVAVHVFR (4-8), KAADDTWEPFASGK (4, 6), TSESGELHGLTTEEEFVEGIYK (4-9), YTIAALLSPYSYSTTAVVTNPK (3-7), YTIAALLSPYSYSTTAVVTNPKE (6)
HPP 50	5	21	AADDTWEPFASGK (4-8), ALGISPFHEHAEVVFTANDSGPR (4-8), CPLMVK (4), GSPAINVAVHVFR (3-8), GSPAINVAVHVFRK (6), KAADDTWEPFASGK (6), RYTIAALLSPYSYSTTAVVTNPK (5-7), TSESGELHGLTTEEEFVEGIYK (4-8), VEIDTK (5), YTIAALLSPYSYSTTAVVTNPK (4-6), YTIAALLSPYSYSTTAVVTNPKE (5-7)
HPP 50	5	22	AADDTWEPFASGK (3-6), ALGISPFHEHAEVVFTANDSGPR (3-6), ALGISPFHEHAEVVFTANDSGPRR (3-5), GPTGTGESKCPLMVK (4), GSPAINVAVHVFR (3-6), GSPAINVAVHVFRK (4-5), KAADDTWEPFASGK (3-5), TSESGELHGLTTEEEFVEGIYK (3-6), TSESGELHGLTTEEEFVEGIYKVEIDTK (3-4), YTIAALLSPYSYSTTAVVTNPK (5), YTIAALLSPYSYSTTAVVTNPKE (3-6)
HPP 50	5	23	AADDTWEPFASGK (3-7), ALGISPFHEHAEVVFTANDSGPR (3-5, 8, 9), ALGISPFHEHAEVVFTANDSGPRR (4), CPLMVKVLDAVR (4-5), GSPAINVAVHVFR (3-7), GSPAINVAVHVFRK (4-5), KAADDTWEPFASGK (3-5), RYTIAALLSPYSYSTTAVVTNPK (4-5, 7, 8), TSESGELHGLTTEEEFVEGIYK (3-5, 7, 8, 9), YTIAALLSPYSYSTTAVVTNPK (3, 5, 7, 8), YTIAALLSPYSYSTTAVVTNPKE (3-4, 6)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	5	24	AADDTWEPFASGK (1, 3, 5), ALGISPFHEHAEVVFTANDSGPR (1-3, 5), GSPAINVAVHVFR (1-2, 5), KAADDTWEPFASGK (1-2), RYTIAALLSPYSYSTTAVVTNPK (1, 3), SYWK (2), TSESGELHGLTTEEEFVEGIYK (1-5), YTIAALLSPYSYSTTAVVTNPK (1-3, 5)
HPP 50	5	25	AADDTWEPFASGK (1-4, 7), ALGISPFHEHAEVVFTANDSGPR (2-4), GSPAINVAVHVFR (1-3, 8), KAADDTWEPFASGK (2), RYTIAALLSPYSYSTTAVVTNPK (2-3), TSESGELHGLTTEEEFVEGIYK (1-7), YTIAALLSPYSYSTTAVVTNPK (2-3, 7), YTIAALLSPYSYSTTAVVTNPKE (3-4)
HPP 50	5	26	AADDTWEPFASGK (1-2), CPLMVK (2), GSPAINVAVHVFR (2), TSESGELHGLTTEEEFVEGIYK (2, 4)
HPP 50	5	27	ALGISPFHEHAEVVFTANDSGPR (2), RYTIAALLSPYSYSTTAVVTNPK (2), TSESGELHGLTTEEEFVEGIYK (2-3), YTIAALLSPYSYSTTAVVTNPK (2)
HPP 50	5	28	AADDTWEPFASGK (2-5), ALGISPFHEHAEVVFTANDSGPR (4), GSPAINVAVHVFR (3-4), GSPAINVAVHVFRK (3), KAADDTWEPFASGK (3), TSESGELHGLTTEEEFVEGIYK (4-8), YTIAALLSPYSYSTTAVVTNPK (4), YTIAALLSPYSYSTTAVVTNPKE (3)
HPP 50	5	29	AADDTWEPFASGK (3-4), ALGISPFHEHAEVVFTANDSGPR (3-4), GSPAINVAVHVFR (3), KAADDTWEPFASGK (3-4), TSESGELHGLTTEEEFVEGIYK (3-6), YTIAALLSPYSYSTTAVVTNPK (3-4)
HPP 50	5	30	AADDTWEPFASGK (3-4), ALGISPFHEHAEVVFTANDSGPR (3), CPLMVK (4), TSESGELHGLTTEEEFVEGIYK (3-4)
HPP 50	6	5	CPLMVK (12)
HPP 50	6	6	CPLMVK (7-8), GPTGTGESKCPLMVK (8)
HPP 50	6	8	YTIAALLSPYSYSTTAVVTNPK (9)
HPP 50	6	9	GSPAINVAVHVFR (8), YTIAALLSPYSYSTTAVVTNPK (10, 13, 14), YTIAALLSPYSYSTTAVVTNPKE (11)
HPP 50	6	10	ALGISPFHEHAEVVFTANDSGPR (8-10), CPLMVK (5), GSPAINVAVHVFR (8), RYTIAALLSPYSYSTTAVVTNPK (8-9), YTIAALLSPYSYSTTAVVTNPK (8-9, 11), YTIAALLSPYSYSTTAVVTNPKE (8-10)
HPP 50	6	11	AADDTWEPFASGK (9-10), ALGISPFHEHAEVVFTANDSGPR (8-11), GSPAINVAVHVFR (9-11), RYTIAALLSPYSYSTTAVVTNPK (8-12), YTIAALLSPYSYSTTAVVTNPK (8-13), YTIAALLSPYSYSTTAVVTNPKE (8-13)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	6	12	AADDTWEPFASGK (9), GSPAINVAVHVFR (8-9), RYTIAALLSPYSYSTTAVVTNPK (7), TSESGELHGLTTEEEFVEGIYK (9-11), YTIAALLSPYSYSTTAVVTNPK (7-10), YTIAALLSPYSYSTTAVVTNPKE (7)
HPP 50	6	13	AADDTWEPFASGK (9, 11, 12, 13, 14), ALGISPFHEHAEVVFTANDSGPR (12-15), GSPAINVAVHVFR (8-11, 13), GSPAINVAVHVFRK (7), KAADDTWEPFASGK (12-13), RYTIAALLSPYSYSTTAVVTNPK (8, 11), TSESGELHGLTTEEEFVEGIYK (10, 12, 13, 14, 15, 16), YTIAALLSPYSYSTTAVVTNPK (8, 11, 12), YTIAALLSPYSYSTTAVVTNPKE (10, 12)
HPP 50	6	14	AADDTWEPFASGK (8-12), ALGISPFHEHAEVVFTANDSGPR (8-12, 15), ALGISPFHEHAEVVFTANDSGPRR (8-9), GSPAINVAVHVFR (8-12), GSPAINVAVHVFRK (8-9), KAADDTWEPFASGK (8-11), RYTIAALLSPYSYSTTAVVTNPK (8), TSESGELHGLTTEEEFVEGIYK (8-16), TSESGELHGLTTEEEFVEGIYKVEIDTK (9), YTIAALLSPYSYSTTAVVTNPK (8-12), YTIAALLSPYSYSTTAVVTNPKE (8-9, 11)
HPP 50	6	15	AADDTWEPFASGK (8-15), ALGISPFHEHAEVVFTANDSGPR (9-16, 18), ALGISPFHEHAEVVFTANDSGPRR (11-12, 14), GPTGTGESKCPLMVK (9-10, 12, 13, 14), GSPAINVAVHVFR (9-13, 15, 16), GSPAINVAVHVFRK (9-14), KAADDTWEPFASGK (8-15), RYTIAALLSPYSYSTTAVVTNPK (11-14, 16), TSESGELHGLTTEEEFVEGIYK (1, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18), TSESGELHGLTTEEEFVEGIYKVEIDTK (9-13), VLDAVRGSPAINVAVHVFR (9-12), YTIAALLSPYSYSTTAVVTNPK (9-14), YTIAALLSPYSYSTTAVVTNPKE (9, 11, 12)
HPP 50	6	16	AADDTWEPFASGK (7-12), ALGISPFHEHAEVVFTANDSGPR (7-12), ALGISPFHEHAEVVFTANDSGPRR (8-9), CPLMVKVLDAVR (11), GPTGTGESKCPLMVK (8-9), GSPAINVAVHVFR (7-11), GSPAINVAVHVFRK (8-9), KAADDTWEPFASGK (7-11), RYTIAALLSPYSYSTTAVVTNPK (9-11), TSESGELHGLTTEEEFVEGIYK (7-11), TSESGELHGLTTEEEFVEGIYKVEIDTK (8-9), VLDAVRGSPAINVAVHVFR (8), YTIAALLSPYSYSTTAVVTNPK (7-10, 12), YTIAALLSPYSYSTTAVVTNPKE (8-12)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	6	17	AADDTWEPFASGK (7-13), ALGISPFHEHAEVVFTANDSGPR (7-13), ALGISPFHEHAEVVFTANDSGPRR (7-9), GPTGTGESK (9), GPTGTGESKCPLMVK (7-10), GSPAINVAVHVFR (7-12), GSPAINVAVHVFRK (7-12), KAADDTWEPFASGK (7-12), RYTIAALLSPYSYSTTAVVTNPK (8-11), TSESGELHGLTTEEEFVEGIYK (8-13), TSESGELHGLTTEEEFVEGIYKVEIDTK (7-8, 11), VEIDTK (10), VLDAVRGSPAINVAVHVFR (7), YTIAALLSPYSYSTTAVVTNPK (8-12), YTIAALLSPYSYSTTAVVTNPKE (7-12)
HPP 50	6	18	AADDTWEPFASGK (5-9), ALGISPFHEHAEVVFTANDSGPR (5-9), ALGISPFHEHAEVVFTANDSGPRR (6-7, 9), CPLMVK (5), CPLMVKVLDAVR (8-9), GPTGTGESKCPLMVK (6-7), GSPAINVAVHVFR (5, 7, 8, 10), GSPAINVAVHVFRK (7, 9), KAADDTWEPFASGK (5-7, 9), RYTIAALLSPYSYSTTAVVTNPK (8), TSESGELHGLTTEEEFVEGIYK (5-11), TSESGELHGLTTEEEFVEGIYKVEIDTK (6-7), VLDAVRGSPAINVAVHVFR (6), YTIAALLSPYSYSTTAVVTNPK (5-8, 10, 12), YTIAALLSPYSYSTTAVVTNPKE (6-7, 9)
HPP 50	6	19	AADDTWEPFASGK (5-11, 13), ALGISPFHEHAEVVFTANDSGPR (5, 7, 8, 9, 10, 11, 12), ALGISPFHEHAEVVFTANDSGPRR (5, 7), CPLMVKVLDAVR (7-9, 12), GPTGTGESKCPLMVK (6-8), GSPAINVAVHVFR (5, 7, 8, 9, 10, 11, 12, 13), GSPAINVAVHVFRK (6-7), KAADDTWEPFASGK (5, 7, 9, 10), RYTIAALLSPYSYSTTAVVTNPK (7, 10, 11), TSESGELHGLTTEEEFVEGIYK (5-13), VLDAVRGSPAINVAVHVFR (6), YTIAALLSPYSYSTTAVVTNPK (5, 7, 8, 9, 10, 12), YTIAALLSPYSYSTTAVVTNPKE (6, 8, 10)
HPP 50	6	20	AADDTWEPFASGK (5-8), ALGISPFHEHAEVVFTANDSGPR (5-9, 11), GPTGTGESKCPLMVK (5-6), GSPAINVAVHVFR (5-9), GSPAINVAVHVFRK (5), KAADDTWEPFASGK (5-6), RYTIAALLSPYSYSTTAVVTNPK (5-6), TSESGELHGLTTEEEFVEGIYK (5-7, 9, 10, 11, 12), YTIAALLSPYSYSTTAVVTNPK (5-6, 8), YTIAALLSPYSYSTTAVVTNPKE (5)
HPP 50	6	21	AADDTWEPFASGK (5-7), ALGISPFHEHAEVVFTANDSGPR (4-9), CPLMVKVLDAVR (7), GPTGTGESKCPLMVK (5), GSPAINVAVHVFR (5-9), GSPAINVAVHVFRK (6), KAADDTWEPFASGK (5, 7), RYTIAALLSPYSYSTTAVVTNPK (4, 6), TSESGELHGLTTEEEFVEGIYK (4-12), TSESGELHGLTTEEEFVEGIYKVEIDTK (5-6), VLDAVR (6), YTIAALLSPYSYSTTAVVTNPK (4-7), YTIAALLSPYSYSTTAVVTNPKE (4-6, 8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	6	22	AADDTWEPFASGK (4-5), ALGISPFHEHAEVVFTANDSGPR (4-5), CPLMVK (4), GPTGTGESKCPLMVK (4), GSPAINVAVHVFR (4-6), GSPAINVAVHVFRK (4-5), KAADDTWEPFASGK (5), RYTIAALLSPYSYSTTAVVTNPK (4-5, 9), TSESGELHGLTTEEEFVEGIYK (3-10), YTIAALLSPYSYSTTAVVTNPK (3-6, 8, 9), YTIAALLSPYSYSTTAVVTNPKE (4-6)
HPP 50	6	23	AADDTWEPFASGK (3-6, 8), ALGISPFHEHAEVVFTANDSGPR (4-5), CPLMVK (4), GSPAINVAVHVFR (3-5), KAADDTWEPFASGK (3), RYTIAALLSPYSYSTTAVVTNPK (3-5), TSESGELHGLTTEEEFVEGIYK (3-6, 8, 9), TSESGELHGLTTEEEFVEGIYKVEIDTK (3-4), VLDAVR (3-4), YTIAALLSPYSYSTTAVVTNPK (3-4), YTIAALLSPYSYSTTAVVTNPKE (3-4, 6, 8)
HPP 50	6	24	AADDTWEPFASGK (2-4, 6), ALGISPFHEHAEVVFTANDSGPR (2-3, 5), GSPAINVAVHVFR (2-3), KAADDTWEPFASGK (2-3), RYTIAALLSPYSYSTTAVVTNPK (2-3), TSESGELHGLTTEEEFVEGIYK (1-6), YTIAALLSPYSYSTTAVVTNPK (2-3), YTIAALLSPYSYSTTAVVTNPKE (2)
HPP 50	6	25	ALGISPFHEHAEVVFTANDSGPR (2-3), KAADDTWEPFASGK (2), TSESGELHGLTTEEEFVEGIYK (1, 3, 4, 5), YTIAALLSPYSYSTTAVVTNPK (2-4), YTIAALLSPYSYSTTAVVTNPKE (3)
HPP 50	7	4	CPLMVK (9-10, 13), GPTGTGESKCPLMVK (9-10, 13)
HPP 50	7	5	GPTGTGESKCPLMVK (9-10, 12, 13, 14)
HPP 50	7	6	CPLMVK (8), GPTGTGESKCPLMVK (7, 9)
HPP 50	7	7	GPTGTGESKCPLMVK (8)
HPP 50	7	8	GPTGTGESKCPLMVK (7), GSPAINVAVHVFR (9-10), RYTIAALLSPYSYSTTAVVTNPK (10, 12), YTIAALLSPYSYSTTAVVTNPK (10-11), YTIAALLSPYSYSTTAVVTNPKE (10, 12)
HPP 50	7	9	GPTGTGESKCPLMVK (6), GSPAINVAVHVFR (9-10), GSPAINVAVHVFRK (9), RYTIAALLSPYSYSTTAVVTNPK (10), YTIAALLSPYSYSTTAVVTNPK (10-11), YTIAALLSPYSYSTTAVVTNPKE (12)
HPP 50	7	10	AADDTWEPFASGK (9), ALGISPFHEHAEVVFTANDSGPR (9-12), GPTGTGESKCPLMVK (5-6), GSPAINVAVHVFR (8, 11), KAADDTWEPFASGK (9), RYTIAALLSPYSYSTTAVVTNPK (8-11), YTIAALLSPYSYSTTAVVTNPK (8-12), YTIAALLSPYSYSTTAVVTNPKE (8, 10)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	7	11	AADDTWEPFASGK (10-12, 16, 17), ALGISPFHEHAEVVFTANDSGPR (10-11), GPTGTGESKCPLMVK (6), GSPAINVAVHVFR (10, 12, 17), KAADDTWEPFASGK (11), RYTIAALLSPYSYSTTAVVTNPK (11-12), TSESGELHGLTTEEEFVEGIYK (17), YTIAALLSPYSYSTTAVVTNPK (8-9, 11, 12), YTIAALLSPYSYSTTAVVTNPKE (10, 12)
HPP 50	7	12	AADDTWEPFASGK (7-10, 13, 14), ALGISPFHEHAEVVFTANDSGPR (8-9, 13, 15), GSPAINVAVHVFR (7, 9, 10, 11, 12, 13, 14, 15), KAADDTWEPFASGK (8, 11, 13), RYTIAALLSPYSYSTTAVVTNPK (11-12), TSESGELHGLTTEEEFVEGIYK (9, 12, 14, 16), YTIAALLSPYSYSTTAVVTNPK (8-11), YTIAALLSPYSYSTTAVVTNPKE (7, 10)
HPP 50	7	13	AADDTWEPFASGK (11, 14, 15, 16, 18, 19), ALGISPFHEHAEVVFTANDSGPR (14-20), ALGISPFHEHAEVVFTANDSGPRR (15), GSPAINVAVHVFR (11, 14, 16, 19, 20), KAADDTWEPFASGK (14-17, 20), RYTIAALLSPYSYSTTAVVTNPK (14-17, 19), TSESGELHGLTTEEEFVEGIYK (11, 13, 14, 15, 16, 17, 18, 19, 20), TSESGELHGLTTEEEFVEGIYKVEIDTK (19), VLDAVR (19), YTIAALLSPYSYSTTAVVTNPK (14-18), YTIAALLSPYSYSTTAVVTNPKE (14-15, 19, 20)
HPP 50	7	14	AADDTWEPFASGK (8-15), ALGISPFHEHAEVVFTANDSGPR (8-15), ALGISPFHEHAEVVFTANDSGPRR (9), GPTGTGESKCPLMVK (14-15), GSPAINVAVHVFR (8-15), GSPAINVAVHVFRK (9-10, 12, 13), KAADDTWEPFASGK (9-12, 14), RYTIAALLSPYSYSTTAVVTNPK (9-11), TSESGELHGLTTEEEFVEGIYK (8-15), TSESGELHGLTTEEEFVEGIYKVEIDTK (9), VLDAVRGSPAINVAVHVFR (14), YTIAALLSPYSYSTTAVVTNPK (9-11, 15), YTIAALLSPYSYSTTAVVTNPKE (9, 11, 12)
HPP 50	7	15	AADDTWEPFASGK (9-17), ALGISPFHEHAEVVFTANDSGPR (9-18), ALGISPFHEHAEVVFTANDSGPRR (9, 12, 13, 14), CPLMVK (13), GPTGTGESKCPLMVK (11-15), GSPAINVAVHVFR (9-17), GSPAINVAVHVFRK (9-10, 12, 16, 17), KAADDTWEPFASGK (9-17), RYTIAALLSPYSYSTTAVVTNPK (10-11, 13, 14, 15, 16, 17), TSESGELHGLTTEEEFVEGIYK (9-18), TSESGELHGLTTEEEFVEGIYKVEIDTK (9, 11, 12), VLDAVRGSPAINVAVHVFR (11, 14), YTIAALLSPYSYSTTAVVTNPK (10-17), YTIAALLSPYSYSTTAVVTNPKE (9, 11, 12, 13, 14, 15, 16)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	7	16	AADDTWEPFASGK (7-13), ALGISPFHEHAEVVFTANDSGPR (7-14), ALGISPFHEHAEVVFTANDSGPRR (8-10), CPLMVK (12), GPTGTGESKCPLMVK (8-10), GSPAINVAVHVFR (7-14), GSPAINVAVHVFRK (7-12), KAADDTWEPFASGK (7-12), RYTIAALLSPYSYSTTAVVTNPK (7, 9, 10, 11, 13), TSESGELHGLTTEEEFVEGIYK (7-17, 21, 22), TSESGELHGLTTEEEFVEGIYKVEIDTK (8, 10), VLDAVRGSPAINVAVHVFR (7-8), YTIAALLSPYSYSTTAVVTNPK (7-14), YTIAALLSPYSYSTTAVVTNPKE (7-14)
HPP 50	7	17	AADDTWEPFASGK (7-14), ALGISPFHEHAEVVFTANDSGPR (7-15), ALGISPFHEHAEVVFTANDSGPRR (8-10), CPLMVK (6, 9, 10, 11), CPLMVKVLDAVR (10), GPTGTGESKCPLMVK (8-10), GSPAINVAVHVFR (7-14), GSPAINVAVHVFRK (8-11, 13), KAADDTWEPFASGK (7-11), RYTIAALLSPYSYSTTAVVTNPK (8-11, 13, 14), TSESGELHGLTTEEEFVEGIYK (7-14, 16, 17, 18), TSESGELHGLTTEEEFVEGIYKVEIDTK (9-10, 12), YTIAALLSPYSYSTTAVVTNPK (7-14), YTIAALLSPYSYSTTAVVTNPKE (8-11, 13, 15)
HPP 50	7	18	AADDTWEPFASGK (5-6, 8, 9), ALGISPFHEHAEVVFTANDSGPR (5-10), ALGISPFHEHAEVVFTANDSGPRR (5, 7), GPTGTGESKCPLMVK (6-7), GSPAINVAVHVFR (6-8), GSPAINVAVHVFRK (5-6), KAADDTWEPFASGK (5-7), RYTIAALLSPYSYSTTAVVTNPK (6), TSESGELHGLTTEEEFVEGIYK (5, 7, 8, 9, 10, 11, 12), TSESGELHGLTTEEEFVEGIYKVEIDTK (5-7), VLDAVRGSPAINVAVHVFR (5-6), YTIAALLSPYSYSTTAVVTNPK (5-8), YTIAALLSPYSYSTTAVVTNPKE (5-8)
HPP 50	7	19	AADDTWEPFASGK (6-11), ALGISPFHEHAEVVFTANDSGPR (7-10), CPLMVKVLDAVR (7), GPTGTGESKCPLMVK (6), GSPAINVAVHVFR (6-8, 10, 12, 18), GSPAINVAVHVFRK (6-8), KAADDTWEPFASGK (6-8), RYTIAALLSPYSYSTTAVVTNPK (9), TSESGELHGLTTEEEFVEGIYK (7-15), VLDAVRGSPAINVAVHVFR (8), YTIAALLSPYSYSTTAVVTNPK (6-9, 11), YTIAALLSPYSYSTTAVVTNPKE (8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	7	20	AADDTWEPFASGK (4-6, 11), ALGISPFHEHAEVVFTANDSGPR (5-7, 10, 11), ALGISPFHEHAEVVFTANDSGPRR (6), CPLMVKVLDAVR (7), GPTGTGESKCPLMVK (5-6), GSPAINVAVHVFR (5-6, 8), GSPAINVAVHVFRK (5-6), KAADDTWEPFASGK (5-6), RYTIAALLSPYSYSTTAVVTNPK (5-6), TSESGELHGLTTEEEFVEGIYK (5-12), TSESGELHGLTTEEEFVEGIYKVEIDTK (6), YTIAALLSPYSYSTTAVVTNPK (4-7), YTIAALLSPYSYSTTAVVTNPKE (6, 11)
HPP 50	7	21	AADDTWEPFASGK (4-7, 9, 11), ALGISPFHEHAEVVFTANDSGPR (5-6, 9, 10, 11, 12), GPTGTGESKCPLMVK (5-6), GSPAINVAVHVFR (5, 8, 9, 12), GSPAINVAVHVFRK (5), KAADDTWEPFASGK (5-6, 8), RYTIAALLSPYSYSTTAVVTNPK (5-6), TSESGELHGLTTEEEFVEGIYK (5-9, 11, 12, 13, 14), YTIAALLSPYSYSTTAVVTNPK (5-6, 10), YTIAALLSPYSYSTTAVVTNPKE (5)
HPP 50	7	22	AADDTWEPFASGK (3-8), ALGISPFHEHAEVVFTANDSGPR (3-5), ALGISPFHEHAEVVFTANDSGPRR (5), GPTGTGESKCPLMVK (4-5), GSPAINVAVHVFR (3-7), GSPAINVAVHVFRK (3-5), KAADDTWEPFASGK (3-5), RYTIAALLSPYSYSTTAVVTNPK (4, 6), TSESGELHGLTTEEEFVEGIYK (3-9), TSESGELHGLTTEEEFVEGIYKVEIDTK (4), VLDAVRGSPAINVAVHVFR (3), YTIAALLSPYSYSTTAVVTNPK (4-7), YTIAALLSPYSYSTTAVVTNPKE (3-8)
HPP 50	7	23	AADDTWEPFASGK (3-6, 9), ALGISPFHEHAEVVFTANDSGPR (3-7, 9), ALGISPFHEHAEVVFTANDSGPRR (3-6), GPTGTGESKCPLMVK (4-5), GSPAINVAVHVFR (3, 5, 6), GSPAINVAVHVFRK (3, 5, 6), KAADDTWEPFASGK (3-7), RYTIAALLSPYSYSTTAVVTNPK (3, 6, 7, 8), TSESGELHGLTTEEEFVEGIYK (3-12), TSESGELHGLTTEEEFVEGIYKVEIDTK (3, 5), VLDAVRGSPAINVAVHVFR (4), YTIAALLSPYSYSTTAVVTNPK (6-8), YTIAALLSPYSYSTTAVVTNPKE (3-7)
HPP 50	7	24	AADDTWEPFASGK (1-7), ALGISPFHEHAEVVFTANDSGPR (1-5, 7), ALGISPFHEHAEVVFTANDSGPRR (1, 3), GSPAINVAVHVFR (1-7), GSPAINVAVHVFRK (3), KAADDTWEPFASGK (1-2, 4), RYTIAALLSPYSYSTTAVVTNPK (1-5, 7), TSESGELHGLTTEEEFVEGIYK (1-7), TSESGELHGLTTEEEFVEGIYKVEIDTK (3-4), YTIAALLSPYSYSTTAVVTNPK (1-7), YTIAALLSPYSYSTTAVVTNPKE (1, 3, 5, 6, 7)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	7	25	AADDTWEPFASGK (1-5), ALGISPFHEHAEVVFTANDSGPR (1-4), ALGISPFHEHAEVVFTANDSGPRR (3), GPTGTGESKCPLMVK (2-3), GSPAINVAVHVFR (1-4), GSPAINVAVHVFRK (2-4), KAADDTWEPFASGK (2-4), RYTIAALLSPYSYSTTAVVTNPK (1-2), TSESGELHGLTTEEEFVEGIYK (1-7), TSESGELHGLTTEEEFVEGIYKVEIDTK (2), YTIAALLSPYSYSTTAVVTNPK (1-3), YTIAALLSPYSYSTTAVVTNPKE (2-3)
HPP 50	7	26	AADDTWEPFASGK (1-3), ALGISPFHEHAEVVFTANDSGPR (1-3), ALGISPFHEHAEVVFTANDSGPRR (2-3), GPTGTGESKCPLMVK (3), GSPAINVAVHVFR (1-3), KAADDTWEPFASGK (1-2), RYTIAALLSPYSYSTTAVVTNPK (1), TSESGELHGLTTEEEFVEGIYK (1-4), VLDAVRGSPAINVAVHVFR (3), YTIAALLSPYSYSTTAVVTNPK (1-2), YTIAALLSPYSYSTTAVVTNPKE (2-3)
HPP 50	7	27	AADDTWEPFASGK (1-4), ALGISPFHEHAEVVFTANDSGPR (2-3), ALGISPFHEHAEVVFTANDSGPRR (1-2), GPTGTGESKCPLMVK (1-2), GSPAINVAVHVFR (1-4), GSPAINVAVHVFRK (2), KAADDTWEPFASGK (1-2), RYTIAALLSPYSYSTTAVVTNPK (2-3), TSESGELHGLTTEEEFVEGIYK (2-5), TSESGELHGLTTEEEFVEGIYKVEIDTK (2), VLDAVRGSPAINVAVHVFR (1), YTIAALLSPYSYSTTAVVTNPK (2-3), YTIAALLSPYSYSTTAVVTNPKE (1, 3)
HPP 50	7	28	AADDTWEPFASGK (3-4), ALGISPFHEHAEVVFTANDSGPR (3-4), CPLMVK (3), GSPAINVAVHVFR (3-4), KAADDTWEPFASGK (3-4), RYTIAALLSPYSYSTTAVVTNPK (3), TSESGELHGLTTEEEFVEGIYK (3-4), VLDAVR (3), YTIAALLSPYSYSTTAVVTNPK (3), YTIAALLSPYSYSTTAVVTNPKE (3)
HPP 50	7	29	AADDTWEPFASGK (3)
HPP 50	7	30	TSESGELHGLTTEEEFVEGIYK (3)
HPP 50	8	6	GPTGTGESKCPLMVK (7, 9)
HPP 50	8	10	GSPAINVAVHVFR (6), GSPAINVAVHVFRK (7), YTIAALLSPYSYSTTAVVTNPK (6-7), YTIAALLSPYSYSTTAVVTNPKE (7-8)
HPP 50	8	11	ALGISPFHEHAEVVFTANDSGPR (9-10), GSPAINVAVHVFR (9), RYTIAALLSPYSYSTTAVVTNPK (7, 9), YTIAALLSPYSYSTTAVVTNPK (8-11), YTIAALLSPYSYSTTAVVTNPKE (7-8)
HPP 50	8	12	AADDTWEPFASGK (7), ALGISPFHEHAEVVFTANDSGPR (6-8), GSPAINVAVHVFR (6-8), RYTIAALLSPYSYSTTAVVTNPK (6-7), YTIAALLSPYSYSTTAVVTNPK (6-8), YTIAALLSPYSYSTTAVVTNPKE (5-8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	8	13	AADDTWEPFASGK (6), ALGISPFHEHAEVVFTANDSGPR (6-8), GSPAINVAVHVFR (6, 9), RYTIAALLSPYSYSTTAVVTNPK (6), YTIAALLSPYSYSTTAVVTNPK (6)
HPP 50	8	14	AADDTWEPFASGK (7), GSPAINVAVHVFR (7), TSESGELHGLTTEEEFVEGIYK (7)
HPP 50	8	15	AADDTWEPFASGK (8-10, 15, 16, 17), ALGISPFHEHAEVVFTANDSGPR (8-11), GPTGTGESKCPLMVK (12), GSPAINVAVHVFR (8-9, 11, 14, 15), GSPAINVAVHVFRK (9), KAADDTWEPFASGK (9-10, 15), RYTIAALLSPYSYSTTAVVTNPK (9), TSESGELHGLTTEEEFVEGIYK (8-12, 14, 15), TSESGELHGLTTEEEFVEGIYKVEIDTK (9), YTIAALLSPYSYSTTAVVTNPK (8-10), YTIAALLSPYSYSTTAVVTNPKE (9-10)
HPP 50	8	16	AADDTWEPFASGK (6-9), ALGISPFHEHAEVVFTANDSGPR (7-9), ALGISPFHEHAEVVFTANDSGPRR (8), CPLMVK (7-8), GPTGTGESKCPLMVK (7-8), GSPAINVAVHVFR (7-9), KAADDTWEPFASGK (7-8), RYTIAALLSPYSYSTTAVVTNPK (7-9), TSESGELHGLTTEEEFVEGIYK (7-9), TSESGELHGLTTEEEFVEGIYKVEIDTK (7-8), YTIAALLSPYSYSTTAVVTNPK (7-8), YTIAALLSPYSYSTTAVVTNPKE (8-9)
HPP 50	8	17	AADDTWEPFASGK (6-9), ALGISPFHEHAEVVFTANDSGPR (6-9), ALGISPFHEHAEVVFTANDSGPRR (7), GPTGTGESKCPLMVK (6-8), GSPAINVAVHVFR (6-8), GSPAINVAVHVFRK (6-9), KAADDTWEPFASGK (6-7), RYTIAALLSPYSYSTTAVVTNPK (7), TSESGELHGLTTEEEFVEGIYK (6-9), TSESGELHGLTTEEEFVEGIYKVEIDTK (7-9), VLDAVRGSPAINVAVHVFR (7), YTIAALLSPYSYSTTAVVTNPK (6-8), YTIAALLSPYSYSTTAVVTNPKE (7-8)
HPP 50	8	18	AADDTWEPFASGK (4-8), ALGISPFHEHAEVVFTANDSGPR (5-8), CPLMVKVLDAVR (6), GSPAINVAVHVFR (4, 6, 7, 8), GSPAINVAVHVFRK (5, 8), KAADDTWEPFASGK (4, 6, 7), RYTIAALLSPYSYSTTAVVTNPK (5-7), TSESGELHGLTTEEEFVEGIYK (5-9), TSESGELHGLTTEEEFVEGIYKVEIDTK (6), VLDAVRGSPAINVAVHVFR (5), YTIAALLSPYSYSTTAVVTNPK (5-8), YTIAALLSPYSYSTTAVVTNPKE (6-7)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	8	19	AADDTWEPFASGK (5-10), ALGISPFHEHAEVVFTANDSGPR (6-10), ALGISPFHEHAEVVFTANDSGPRR (7-8), CPLMVK (6), GPTGTGESKCPLMVK (7), GSPAINVAVHVFR (6-9), GSPAINVAVHVFRK (6), KAADDTWEPFASGK (5-8), RYTIAALLSPYSYSTTAVVTNPK (5-6, 8, 9, 11), TSESGELHGLTTEEEFVEGIYK (5-12), TSESGELHGLTTEEEFVEGIYKVEIDTK (6-8), YTIAALLSPYSYSTTAVVTNPK (5-12), YTIAALLSPYSYSTTAVVTNPKE (5-9)
HPP 50	8	20	AADDTWEPFASGK (4-7), ALGISPFHEHAEVVFTANDSGPR (6-7), ALGISPFHEHAEVVFTANDSGPRR (7), CPLMVK (5), CPLMVKVLDAVR (6), GSPAINVAVHVFR (4, 6, 7), GSPAINVAVHVFRK (7), KAADDTWEPFASGK (6-7), RYTIAALLSPYSYSTTAVVTNPK (5-6), TSESGELHGLTTEEEFVEGIYK (4-7, 9), YTIAALLSPYSYSTTAVVTNPK (4, 6), YTIAALLSPYSYSTTAVVTNPKE (5-7)
HPP 50	8	21	AADDTWEPFASGK (4-8), ALGISPFHEHAEVVFTANDSGPR (5-7, 10), ALGISPFHEHAEVVFTANDSGPRR (8), GSPAINVAVHVFR (5-6), KAADDTWEPFASGK (5-7), RYTIAALLSPYSYSTTAVVTNPK (4-5, 7), TSESGELHGLTTEEEFVEGIYK (4-9, 11), YTIAALLSPYSYSTTAVVTNPK (4-7, 10, 11), YTIAALLSPYSYSTTAVVTNPKE (5-7, 10)
HPP 50	8	22	AADDTWEPFASGK (3, 5, 6, 7, 10, 12), ALGISPFHEHAEVVFTANDSGPR (3-7), CPLMVK (4), GSPAINVAVHVFR (3-6), KAADDTWEPFASGK (4-5), RYTIAALLSPYSYSTTAVVTNPK (3-5), TSESGELHGLTTEEEFVEGIYK (3-10), YTIAALLSPYSYSTTAVVTNPK (3, 5, 6), YTIAALLSPYSYSTTAVVTNPKE (3, 7)
HPP 50	8	23	AADDTWEPFASGK (3-5), ALGISPFHEHAEVVFTANDSGPR (3-4), GPTGTGESKCPLMVK (4), GSPAINVAVHVFR (3, 7), KAADDTWEPFASGK (3, 5), TSESGELHGLTTEEEFVEGIYK (3, 6), VLDAVRGSPAINVAVHVFR (4), YTIAALLSPYSYSTTAVVTNPK (3), YTIAALLSPYSYSTTAVVTNPKE (3-4)
HPP 50	8	24	AADDTWEPFASGK (1-4, 6), ALGISPFHEHAEVVFTANDSGPR (1-5, 8), GSPAINVAVHVFR (1-2, 5, 7), KAADDTWEPFASGK (1-3), RYTIAALLSPYSYSTTAVVTNPK (2, 5), TSESGELHGLTTEEEFVEGIYK (1-5, 8), YTIAALLSPYSYSTTAVVTNPK (2-5, 8), YTIAALLSPYSYSTTAVVTNPKE (3-5)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	8	25	AADDTWEPFASGK (2), ALGISPFHEHAEVVFTANDSGPR (2), GSPAINVAVHVFR (2-3), GSPAINVAVHVFRK (3), RYTIAALLSPYSYSTTAVVTNPK (3), TSESGELHGLTTEEEFVEGIYK (1-3), YTIAALLSPYSYSTTAVVTNPK (2-3)
HPP 50	8	30	GSPAINVAVHVFR (3)
HPP 50	9	5	CPLMVK (9, 13), GPTGTGESKCPLMVK (9, 13)
HPP 50	9	6	CPLMVK (7), GPTGTGESKCPLMVK (7-8)
HPP 50	9	9	RYTIAALLSPYSYSTTAVVTNPK (10-11), YTIAALLSPYSYSTTAVVTNPK (10-11, 13), YTIAALLSPYSYSTTAVVTNPKE (10-11)
HPP 50	9	10	GSPAINVAVHVFR (8), YTIAALLSPYSYSTTAVVTNPK (9)
HPP 50	9	11	AADDTWEPFASGK (11), ALGISPFHEHAEVVFTANDSGPRR (11), GSPAINVAVHVFRK (12), RYTIAALLSPYSYSTTAVVTNPK (9-10), YTIAALLSPYSYSTTAVVTNPK (9-10), YTIAALLSPYSYSTTAVVTNPKE (11)
HPP 50	9	12	ALGISPFHEHAEVVFTANDSGPR (8), TSESGELHGLTTEEEFVEGIYK (14), YTIAALLSPYSYSTTAVVTNPK (8)
HPP 50	9	13	AADDTWEPFASGK (15, 17, 18), ALGISPFHEHAEVVFTANDSGPR (15-17), GSPAINVAVHVFR (14-16), KAADDTWEPFASGK (15-16), RYTIAALLSPYSYSTTAVVTNPK (14-16), TSESGELHGLTTEEEFVEGIYK (12, 14, 15), TSESGELHGLTTEEEFVEGIYKVEIDTK (15), YTIAALLSPYSYSTTAVVTNPK (15-18), YTIAALLSPYSYSTTAVVTNPKE (14, 18)
HPP 50	9	14	AADDTWEPFASGK (8-9, 12, 15), ALGISPFHEHAEVVFTANDSGPR (9, 12, 14), GPTGTGESKCPLMVK (14), GSPAINVAVHVFR (10-14), KAADDTWEPFASGK (11-13), RYTIAALLSPYSYSTTAVVTNPK (11-12, 14), TSESGELHGLTTEEEFVEGIYK (8-15), YTIAALLSPYSYSTTAVVTNPK (10-11, 13, 14)
HPP 50	9	15	AADDTWEPFASGK (9-17, 19), ALGISPFHEHAEVVFTANDSGPR (9-17), ALGISPFHEHAEVVFTANDSGPRR (12, 14), CPLMVK (10-11), GPTGTGESKCPLMVK (12-15), GSPAINVAVHVFR (10-17), GSPAINVAVHVFRK (10-12, 14, 15), KAADDTWEPFASGK (10-17), RYTIAALLSPYSYSTTAVVTNPK (9, 11, 13, 14, 16, 17), TSESGELHGLTTEEEFVEGIYK (8-19), YTIAALLSPYSYSTTAVVTNPK (9-11, 13, 14, 15, 16, 17), YTIAALLSPYSYSTTAVVTNPKE (12, 14)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	9	16	AADDTWEPFASGK (7-16), ALGISPFHEHAEVVFTANDSGPR (7-15), ALGISPFHEHAEVVFTANDSGPRR (9), CPLMVK (9), CPLMVKVLDAVR (10-11), GPTGTGESK (7), GPTGTGESKCPLMVK (8), GSPAINVAVHVFR (7-10, 12, 13, 14), GSPAINVAVHVFRK (7-8), KAADDTWEPFASGK (7-15), RYTIAALLSPYSYSTTAVVTNPK (7, 10, 11, 12, 13, 14, 16, 17), TSESGELHGLTTEEEFVEGIYK (7-17), TSESGELHGLTTEEEFVEGIYKVEIDTK (9-10, 14), VLDAVR (10, 14), VLDAVRGSPAINVAVHVFR (10), YTIAALLSPYSYSTTAVVTNPK (7-17), YTIAALLSPYSYSTTAVVTNPKE (7-16)
HPP 50	9	17	AADDTWEPFASGK (7-11, 14, 15), ALGISPFHEHAEVVFTANDSGPR (7-12, 14, 15), ALGISPFHEHAEVVFTANDSGPRR (8), GPTGTGESKCPLMVK (8), GSPAINVAVHVFR (7-14), GSPAINVAVHVFRK (9), KAADDTWEPFASGK (7, 9, 11, 13), RYTIAALLSPYSYSTTAVVTNPK (7, 9, 10, 11, 12), TSESGELHGLTTEEEFVEGIYK (7-10, 12, 13, 14, 15, 16, 17, 18), TSESGELHGLTTEEEFVEGIYKVEIDTK (8-10), YTIAALLSPYSYSTTAVVTNPK (7-12, 14, 15), YTIAALLSPYSYSTTAVVTNPKE (7-12, 16)
HPP 50	9	18	AADDTWEPFASGK (6-7, 9), ALGISPFHEHAEVVFTANDSGPR (6-9, 11), ALGISPFHEHAEVVFTANDSGPRR (6-7), CPLMVKVLDAVR (7-8), GPTGTGESKCPLMVK (7), GSPAINVAVHVFR (6-8), GSPAINVAVHVFRK (7), KAADDTWEPFASGK (7), RYTIAALLSPYSYSTTAVVTNPK (6-9), TSESGELHGLTTEEEFVEGIYK (5-10, 13), TSESGELHGLTTEEEFVEGIYKVEIDTK (6-7), YTIAALLSPYSYSTTAVVTNPK (6-9, 12), YTIAALLSPYSYSTTAVVTNPKE (6-8)
HPP 50	9	19	AADDTWEPFASGK (5-8, 12), ALGISPFHEHAEVVFTANDSGPR (5-8, 10, 11), GSPAINVAVHVFR (5-7), KAADDTWEPFASGK (5), RYTIAALLSPYSYSTTAVVTNPK (5-7), TSESGELHGLTTEEEFVEGIYK (5-13), YTIAALLSPYSYSTTAVVTNPK (6-7, 11, 12, 13), YTIAALLSPYSYSTTAVVTNPKE (6-10, 12)
HPP 50	9	20	AADDTWEPFASGK (5-8, 10, 11), ALGISPFHEHAEVVFTANDSGPR (4-8), CPLMVK (6), GSPAINVAVHVFR (5-7), KAADDTWEPFASGK (6), RYTIAALLSPYSYSTTAVVTNPK (5-7), TSESGELHGLTTEEEFVEGIYK (4-12, 15), VEIDTK (5-6), YTIAALLSPYSYSTTAVVTNPK (5-9), YTIAALLSPYSYSTTAVVTNPKE (4-8, 11)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	9	21	AADDTWEPFASGK (5-7), ALGISPFHEHAEVVFTANDSGPR (4-8), CPLMVK (5), GSPAINVAVHVFR (4-7), KAADDTWEPFASGK (4), RYTIAALLSPYSYSTTAVVTNPK (6-7), TSESGELHGLTTEEEFVEGIYK (4-8, 10), VEIDTK (6-8), YTIAALLSPYSYSTTAVVTNPK (5-6), YTIAALLSPYSYSTTAVVTNPKE (4-6)
HPP 50	9	22	AADDTWEPFASGK (4-5), ALGISPFHEHAEVVFTANDSGPR (3-4), GSPAINVAVHVFR (3), KAADDTWEPFASGK (4), RYTIAALLSPYSYSTTAVVTNPK (4), TSESGELHGLTTEEEFVEGIYK (3-8), YTIAALLSPYSYSTTAVVTNPK (3-4)
HPP 50	9	23	AADDTWEPFASGK (3-5, 7), ALGISPFHEHAEVVFTANDSGPR (4), KAADDTWEPFASGK (4), RYTIAALLSPYSYSTTAVVTNPK (3-4), TSESGELHGLTTEEEFVEGIYK (3-5, 7, 10), YTIAALLSPYSYSTTAVVTNPK (3-5), YTIAALLSPYSYSTTAVVTNPKE (3-4)
HPP 50	9	24	AADDTWEPFASGK (1, 5), ALGISPFHEHAEVVFTANDSGPR (2), KAADDTWEPFASGK (1), RYTIAALLSPYSYSTTAVVTNPK (2), TSESGELHGLTTEEEFVEGIYK (1-2, 4, 5), YTIAALLSPYSYSTTAVVTNPK (1-2), YTIAALLSPYSYSTTAVVTNPKE (1-2, 5)
HPP 50	9	25	AADDTWEPFASGK (1), ALGISPFHEHAEVVFTANDSGPR (3-4), GSPAINVAVHVFR (3), TSESGELHGLTTEEEFVEGIYK (2, 6), YTIAALLSPYSYSTTAVVTNPK (2), YTIAALLSPYSYSTTAVVTNPKE (3)
HPP 50	9	26	AADDTWEPFASGK (2), GSPAINVAVHVFR (2), KAADDTWEPFASGK (2), TSESGELHGLTTEEEFVEGIYK (2)
HPP 50	9	27	AADDTWEPFASGK (1)
HPP 50	9	28	AADDTWEPFASGK (3)
HPP 50	9	30	AADDTWEPFASGK (3-4), TSESGELHGLTTEEEFVEGIYK (3-4), VLDAVR (4)
HPP 50	10	5	GPTGTGESKCPLMVK (16)
HPP 50	10	9	YTIAALLSPYSYSTTAVVTNPKE (12)
HPP 50	10	14	AADDTWEPFASGK (9), TSESGELHGLTTEEEFVEGIYK (9, 11)
HPP 50	10	15	AADDTWEPFASGK (9, 11, 12, 13, 14), ALGISPFHEHAEVVFTANDSGPR (9-15), GSPAINVAVHVFR (10-14), GSPAINVAVHVFRK (9), KAADDTWEPFASGK (10-12), RYTIAALLSPYSYSTTAVVTNPK (9-10, 12), TSESGELHGLTTEEEFVEGIYK (8-14), YTIAALLSPYSYSTTAVVTNPK (8-12, 14), YTIAALLSPYSYSTTAVVTNPKE (9, 11, 12, 13)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	10	16	AADDTWEPFASGK (9-12), ALGISPFHEHAEVVFTANDSGPR (8-10, 12), GSPAINVAVHVFR (7-10), GSPAINVAVHVFRK (8), KAADDTWEPFASGK (9), RYTIAALLSPYSYSTTAVVTNPK (9), TSESGELHGLTTEEEFVEGIYK (7-9, 11), YTIAALLSPYSYSTTAVVTNPK (9-10, 12), YTIAALLSPYSYSTTAVVTNPKE (8-9)
HPP 50	10	17	AADDTWEPFASGK (7-11, 13), ALGISPFHEHAEVVFTANDSGPR (7-10), ALGISPFHEHAEVVFTANDSGPRR (9), CPLMVK (9), CPLMVKVLDAVR (11), GPTGTGESKCPLMVK (8-9), GSPAINVAVHVFR (7-11), GSPAINVAVHVFRK (8-9), KAADDTWEPFASGK (9-10), RYTIAALLSPYSYSTTAVVTNPK (7-9), TSESGELHGLTTEEEFVEGIYK (7-11), TSESGELHGLTTEEEFVEGIYKVEIDTK (9), YTIAALLSPYSYSTTAVVTNPK (7-11), YTIAALLSPYSYSTTAVVTNPKE (7-11)
HPP 50	10	18	AADDTWEPFASGK (5-7), ALGISPFHEHAEVVFTANDSGPR (6-7), CPLMVKVLDAVR (7-8), GSPAINVAVHVFR (8), TSESGELHGLTTEEEFVEGIYK (6-9), YTIAALLSPYSYSTTAVVTNPK (6-7)
HPP 50	10	19	AADDTWEPFASGK (5, 7, 8), ALGISPFHEHAEVVFTANDSGPR (7-8), GSPAINVAVHVFR (7-8), RYTIAALLSPYSYSTTAVVTNPK (8), TSESGELHGLTTEEEFVEGIYK (5, 7, 8, 10, 12, 13), YTIAALLSPYSYSTTAVVTNPK (7)
HPP 50	10	20	AADDTWEPFASGK (6-8), ALGISPFHEHAEVVFTANDSGPR (4-5, 7), GSPAINVAVHVFR (7, 9), KAADDTWEPFASGK (6), RYTIAALLSPYSYSTTAVVTNPK (7), TSESGELHGLTTEEEFVEGIYK (4-9), YTIAALLSPYSYSTTAVVTNPK (7-8), YTIAALLSPYSYSTTAVVTNPKE (7)
HPP 50	10	21	ALGISPFHEHAEVVFTANDSGPR (8), TSESGELHGLTTEEEFVEGIYK (4-9), YTIAALLSPYSYSTTAVVTNPK (4), YTIAALLSPYSYSTTAVVTNPKE (8)
HPP 50	10	22	AADDTWEPFASGK (4-5), ALGISPFHEHAEVVFTANDSGPR (7), GSPAINVAVHVFR (4-5), KAADDTWEPFASGK (4), RYTIAALLSPYSYSTTAVVTNPK (4), TSESGELHGLTTEEEFVEGIYK (4-5, 7), YTIAALLSPYSYSTTAVVTNPK (4-5, 7), YTIAALLSPYSYSTTAVVTNPKE (5)
HPP 50	10	23	AADDTWEPFASGK (4-5), GSPAINVAVHVFR (4-5), TSESGELHGLTTEEEFVEGIYK (4-5, 11), YTIAALLSPYSYSTTAVVTNPK (5), YTIAALLSPYSYSTTAVVTNPKE (5)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	10	24	AADDTWEPFASGK (1-3), ALGISPFHEHAEVVFTANDSGPR (2-3), GSPAINVAVHVFR (2-3), KAADDTWEPFASGK (2), RYTIAALLSPYSYSTTAVVTNPK (2-3), TSESGELHGLTTEEEFVEGIYK (1-3), YTIAALLSPYSYSTTAVVTNPK (2-3)
HPP 50	10	25	GSPAINVAVHVFR (1, 3), TSESGELHGLTTEEEFVEGIYK (1, 4)
HPP 50	10	26	AADDTWEPFASGK (1)
HPP 50	10	27	TSESGELHGLTTEEEFVEGIYK (2)
HPP 50	10	28	TSESGELHGLTTEEEFVEGIYK (4)
HPP 50	10	29	TSESGELHGLTTEEEFVEGIYK (3)
HPP 50	11	6	GPTGTGESKCPLMVK (8)
HPP 50	11	8	RYTIAALLSPYSYSTTAVVTNPK (12), YTIAALLSPYSYSTTAVVTNPK (11)
HPP 50	11	9	YTIAALLSPYSYSTTAVVTNPK (11-12)
HPP 50	11	11	ALGISPFHEHAEVVFTANDSGPR (11)
HPP 50	11	13	TSESGELHGLTTEEEFVEGIYK (18)
HPP 50	11	14	AADDTWEPFASGK (9-13), ALGISPFHEHAEVVFTANDSGPR (9, 11, 12, 13), CPLMVK (11), GSPAINVAVHVFR (9-13), GSPAINVAVHVFRK (9), KAADDTWEPFASGK (9-12), RYTIAALLSPYSYSTTAVVTNPK (9-12), TSESGELHGLTTEEEFVEGIYK (9-13, 15), YTIAALLSPYSYSTTAVVTNPK (9-13), YTIAALLSPYSYSTTAVVTNPKE (12)
HPP 50	11	15	AADDTWEPFASGK (10-12), ALGISPFHEHAEVVFTANDSGPR (10-14, 17, 18), CPLMVK (14), GSPAINVAVHVFR (7, 9, 10, 11, 12, 14, 15, 16), KAADDTWEPFASGK (11, 14), RYTIAALLSPYSYSTTAVVTNPK (12, 14, 15, 16), TSESGELHGLTTEEEFVEGIYK (10-17), TSESGELHGLTTEEEFVEGIYKVEIDTK (16), YTIAALLSPYSYSTTAVVTNPK (11-12, 15, 16), YTIAALLSPYSYSTTAVVTNPKE (12-13, 15, 17)
HPP 50	11	16	AADDTWEPFASGK (8-13, 15), ALGISPFHEHAEVVFTANDSGPR (8-11), ALGISPFHEHAEVVFTANDSGPRR (8-10), CPLMVK (11), GPTGTGESKCPLMVK (10), GSPAINVAVHVFR (8-12), GSPAINVAVHVFRK (9-10), KAADDTWEPFASGK (8, 10, 11), RYTIAALLSPYSYSTTAVVTNPK (9-11, 13), TSESGELHGLTTEEEFVEGIYK (7-15), TSESGELHGLTTEEEFVEGIYKVEIDTK (10), VLDAVR (11), YTIAALLSPYSYSTTAVVTNPK (8-9, 11, 12, 13), YTIAALLSPYSYSTTAVVTNPKE (8-13, 15)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	11	17	AADDTWEPFASGK (7-12), ALGISPFHEHAEVVFTANDSGPR (8-13, 16), CPLMVKVLDAVR (12), GPTGTGESKCPLMVK (10), GSPAINVAVHVFR (7-12, 14), GSPAINVAVHVFRK (10), KAADDTWEPFASGK (9-11), RYTIAALLSPYSYSTTAVVTNPK (11), TSESGELHGLTTEEEFVEGIYK (7-12, 14, 15, 16, 17, 18), TSESGELHGLTTEEEFVEGIYKVEIDTK (11), VEIDTK (9), VLDAVR (10), YTIAALLSPYSYSTTAVVTNPK (7-12, 14), YTIAALLSPYSYSTTAVVTNPKE (9-11, 13)
HPP 50	11	18	AADDTWEPFASGK (7), ALGISPFHEHAEVVFTANDSGPR (7, 9, 12, 13), GSPAINVAVHVFR (6-9), GSPAINVAVHVFRK (7), RYTIAALLSPYSYSTTAVVTNPK (9-10), TSESGELHGLTTEEEFVEGIYK (7-9, 11, 12, 13, 14), YTIAALLSPYSYSTTAVVTNPK (7, 9, 10, 11, 12), YTIAALLSPYSYSTTAVVTNPKE (7-8, 12)
HPP 50	11	19	AADDTWEPFASGK (6-11), ALGISPFHEHAEVVFTANDSGPR (7-11), CPLMVK (7), GSPAINVAVHVFR (7-9, 11), KAADDTWEPFASGK (8-9, 11), RYTIAALLSPYSYSTTAVVTNPK (7-10), TSESGELHGLTTEEEFVEGIYK (6-11, 13, 14, 15, 16), YTIAALLSPYSYSTTAVVTNPK (7, 9, 10, 11), YTIAALLSPYSYSTTAVVTNPKE (10)
HPP 50	11	20	AADDTWEPFASGK (5, 7), ALGISPFHEHAEVVFTANDSGPR (5, 8), CPLMVKVLDAVR (7), GSPAINVAVHVFR (8), KAADDTWEPFASGK (7), TSESGELHGLTTEEEFVEGIYK (5-9), YTIAALLSPYSYSTTAVVTNPK (5-9)
HPP 50	11	21	AADDTWEPFASGK (6), ALGISPFHEHAEVVFTANDSGPR (6), GSPAINVAVHVFR (6), RYTIAALLSPYSYSTTAVVTNPK (6, 8), TSESGELHGLTTEEEFVEGIYK (4-10), YTIAALLSPYSYSTTAVVTNPK (5-6, 8), YTIAALLSPYSYSTTAVVTNPKE (6)
HPP 50	11	22	AADDTWEPFASGK (4-7), CPLMVK (5), GSPAINVAVHVFR (5), KAADDTWEPFASGK (3), RYTIAALLSPYSYSTTAVVTNPK (4-5), TSESGELHGLTTEEEFVEGIYK (4-7), YTIAALLSPYSYSTTAVVTNPK (4-7), YTIAALLSPYSYSTTAVVTNPKE (5-6)
HPP 50	11	23	AADDTWEPFASGK (4-5), ALGISPFHEHAEVVFTANDSGPR (5, 7), RYTIAALLSPYSYSTTAVVTNPK (4-5), TSESGELHGLTTEEEFVEGIYK (4-7), TSESGELHGLTTEEEFVEGIYKVEIDTK (5), YTIAALLSPYSYSTTAVVTNPK (4-5), YTIAALLSPYSYSTTAVVTNPKE (5)
HPP 50	11	24	AADDTWEPFASGK (1), ALGISPFHEHAEVVFTANDSGPR (3), TSESGELHGLTTEEEFVEGIYK (2-4), YTIAALLSPYSYSTTAVVTNPK (3)
HPP 50	11	25	AADDTWEPFASGK (3), ALGISPFHEHAEVVFTANDSGPR (3), GSPAINVAVHVFR (3), YTIAALLSPYSYSTTAVVTNPK (3)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	11	29	TSESGELHGLTTEEEFVEGIYK (3)
HPP 50	12	9	YTIAALLSPYSYSTTAVVTNPK (8)
HPP 50	12	13	TSESGELHGLTTEEEFVEGIYK (17)
HPP 50	12	14	AADDTWEPFASGK (9), ALGISPFHEHAEVVFTANDSGPR (9), ALGISPFHEHAEVVFTANDSGPRR (9, 11), GSPAINVAVHVFR (8-9), TSESGELHGLTTEEEFVEGIYK (8-11), YTIAALLSPYSYSTTAVVTNPK (8), YTIAALLSPYSYSTTAVVTNPKE (8-9)
HPP 50	12	15	AADDTWEPFASGK (10), ALGISPFHEHAEVVFTANDSGPR (11-14, 16), ALGISPFHEHAEVVFTANDSGPRR (12), GSPAINVAVHVFR (10-11, 13), KAADDTWEPFASGK (10), RYTIAALLSPYSYSTTAVVTNPK (11), TSESGELHGLTTEEEFVEGIYK (10-16), YTIAALLSPYSYSTTAVVTNPK (10-13), YTIAALLSPYSYSTTAVVTNPKE (10)
HPP 50	12	16	AADDTWEPFASGK (9-10), ALGISPFHEHAEVVFTANDSGPR (8-10), ALGISPFHEHAEVVFTANDSGPRR (8), GSPAINVAVHVFR (8-9), KAADDTWEPFASGK (8-9), TSESGELHGLTTEEEFVEGIYK (7, 9, 10, 12, 13), YTIAALLSPYSYSTTAVVTNPK (9), YTIAALLSPYSYSTTAVVTNPKE (8-9)
HPP 50	12	17	AADDTWEPFASGK (8), ALGISPFHEHAEVVFTANDSGPR (7-9), GSPAINVAVHVFR (8), KAADDTWEPFASGK (8), RYTIAALLSPYSYSTTAVVTNPK (8), TSESGELHGLTTEEEFVEGIYK (8, 10, 11, 12), YTIAALLSPYSYSTTAVVTNPK (8)
HPP 50	12	18	AADDTWEPFASGK (5, 7), ALGISPFHEHAEVVFTANDSGPR (5, 7), GSPAINVAVHVFR (5, 7), TSESGELHGLTTEEEFVEGIYK (5, 7, 8, 9), YTIAALLSPYSYSTTAVVTNPK (5-7), YTIAALLSPYSYSTTAVVTNPKE (5)
HPP 50	12	19	AADDTWEPFASGK (6), ALGISPFHEHAEVVFTANDSGPR (7-8), GSPAINVAVHVFR (7), TSESGELHGLTTEEEFVEGIYK (7-9, 12, 13), YTIAALLSPYSYSTTAVVTNPK (7), YTIAALLSPYSYSTTAVVTNPKE (7)
HPP 50	12	20	AADDTWEPFASGK (4-8), ALGISPFHEHAEVVFTANDSGPR (6-7), GSPAINVAVHVFR (4, 6, 7), RYTIAALLSPYSYSTTAVVTNPK (5, 7), TSESGELHGLTTEEEFVEGIYK (4-7, 9), TSESGELHGLTTEEEFVEGIYKVEIDTK (8), YTIAALLSPYSYSTTAVVTNPK (5-7), YTIAALLSPYSYSTTAVVTNPKE (5, 7, 8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	12	21	AADDTWEPFASGK (5-7, 9), ALGISPFHEHAEVVFTANDSGPR (5, 7, 8), GSPAINVAVHVFR (7), RYTIAALLSPYSYSTTAVVTNPK (6), TSESGELHGLTTEEEFVEGIYK (5-10), YTIAALLSPYSYSTTAVVTNPK (6-8), YTIAALLSPYSYSTTAVVTNPKE (6-8)
HPP 50	12	22	AADDTWEPFASGK (3), ALGISPFHEHAEVVFTANDSGPR (3), GSPAINVAVHVFR (3), TSESGELHGLTTEEEFVEGIYK (3)
HPP 50	12	23	AADDTWEPFASGK (3-4), GSPAINVAVHVFR (3), TSESGELHGLTTEEEFVEGIYK (5, 7)
HPP 50	12	25	ALGISPFHEHAEVVFTANDSGPR (1), GSPAINVAVHVFR (3), TSESGELHGLTTEEEFVEGIYK (3)
HPP 50	13	10	YTIAALLSPYSYSTTAVVTNPKE (9)
HPP 50	13	14	AADDTWEPFASGK (9), ALGISPFHEHAEVVFTANDSGPR (9-10), KAADDTWEPFASGK (9), RYTIAALLSPYSYSTTAVVTNPK (9), TSESGELHGLTTEEEFVEGIYK (9-12), YTIAALLSPYSYSTTAVVTNPK (9-10)
HPP 50	13	15	AADDTWEPFASGK (11, 13), ALGISPFHEHAEVVFTANDSGPR (11-14), CPLMVK (12), GSPAINVAVHVFR (10-13), KAADDTWEPFASGK (13), RYTIAALLSPYSYSTTAVVTNPK (14), TSESGELHGLTTEEEFVEGIYK (9-10, 13, 15), VLDAVRGSPAINVAVHVFR (10), YTIAALLSPYSYSTTAVVTNPK (11, 13, 14), YTIAALLSPYSYSTTAVVTNPKE (13)
HPP 50	13	16	AADDTWEPFASGK (9), ALGISPFHEHAEVVFTANDSGPR (7-9), ALGISPFHEHAEVVFTANDSGPRR (8-9), GSPAINVAVHVFR (8-9), GSPAINVAVHVFRK (9), KAADDTWEPFASGK (7-9), RYTIAALLSPYSYSTTAVVTNPK (9), TSESGELHGLTTEEEFVEGIYK (7-10), VLDAVRGSPAINVAVHVFR (7), YTIAALLSPYSYSTTAVVTNPK (7-9), YTIAALLSPYSYSTTAVVTNPKE (8-9)
HPP 50	13	17	AADDTWEPFASGK (9, 11, 12), ALGISPFHEHAEVVFTANDSGPR (8-13), GPTGTGESKCPLMVK (10), GSPAINVAVHVFR (8-10), GSPAINVAVHVFRK (10), KAADDTWEPFASGK (9-11), RYTIAALLSPYSYSTTAVVTNPK (12), TSESGELHGLTTEEEFVEGIYK (8-12, 14), YTIAALLSPYSYSTTAVVTNPK (9-12), YTIAALLSPYSYSTTAVVTNPKE (10, 12)
HPP 50	13	18	AADDTWEPFASGK (5, 7, 8), ALGISPFHEHAEVVFTANDSGPR (7-8), GSPAINVAVHVFR (6-9), KAADDTWEPFASGK (6, 8), TSESGELHGLTTEEEFVEGIYK (5-7), YTIAALLSPYSYSTTAVVTNPK (6-7, 9, 10), YTIAALLSPYSYSTTAVVTNPKE (7-8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	13	19	AADDTWEPFASGK (7), ALGISPFHEHAEVVFTANDSGPR (8-9), ALGISPFHEHAEVVFTANDSGPRR (8), GSPAINVAVHVFR (6-8), KAADDTWEPFASGK (6-7), RYTIAALLSPYSYSTTAVVTNPK (11), TSESGELHGLTTEEEFVEGIYK (6, 9, 10, 11, 12), YTIAALLSPYSYSTTAVVTNPK (6, 11)
HPP 50	13	20	AADDTWEPFASGK (5-6), ALGISPFHEHAEVVFTANDSGPR (5-6), GSPAINVAVHVFR (5-8), TSESGELHGLTTEEEFVEGIYK (6-8), YTIAALLSPYSYSTTAVVTNPK (6)
HPP 50	13	21	AADDTWEPFASGK (5-9), ALGISPFHEHAEVVFTANDSGPR (5-12), GSPAINVAVHVFR (5-6, 8), KAADDTWEPFASGK (5), RYTIAALLSPYSYSTTAVVTNPK (6-7), TSESGELHGLTTEEEFVEGIYK (5-12, 14), YTIAALLSPYSYSTTAVVTNPK (6-10), YTIAALLSPYSYSTTAVVTNPKE (6)
HPP 50	13	22	AADDTWEPFASGK (3-5, 7), ALGISPFHEHAEVVFTANDSGPR (7), GSPAINVAVHVFR (3-5), KAADDTWEPFASGK (4), RYTIAALLSPYSYSTTAVVTNPK (4-5), TSESGELHGLTTEEEFVEGIYK (4-7), YTIAALLSPYSYSTTAVVTNPK (3-5, 7), YTIAALLSPYSYSTTAVVTNPKE (5)
HPP 50	13	23	AADDTWEPFASGK (4-5), ALGISPFHEHAEVVFTANDSGPR (5), GSPAINVAVHVFR (3-4), KAADDTWEPFASGK (4), RYTIAALLSPYSYSTTAVVTNPK (5), TSESGELHGLTTEEEFVEGIYK (5-8), YTIAALLSPYSYSTTAVVTNPK (4-5, 7), YTIAALLSPYSYSTTAVVTNPKE (5)
HPP 50	13	24	AADDTWEPFASGK (2-3), GSPAINVAVHVFR (3), TSESGELHGLTTEEEFVEGIYK (3), YTIAALLSPYSYSTTAVVTNPKE (3)
HPP 50	13	25	AADDTWEPFASGK (3), GSPAINVAVHVFR (3), TSESGELHGLTTEEEFVEGIYK (3-5), YTIAALLSPYSYSTTAVVTNPK (3)
HPP 50	13	26	TSESGELHGLTTEEEFVEGIYK (3)
HPP 50	14	9	YTIAALLSPYSYSTTAVVTNPK (11-12)
HPP 50	14	13	AADDTWEPFASGK (15), ALGISPFHEHAEVVFTANDSGPR (15), GSPAINVAVHVFR (15), GSPAINVAVHVFRK (15), KAADDTWEPFASGK (15), TSESGELHGLTTEEEFVEGIYK (12-13, 15, 16), YTIAALLSPYSYSTTAVVTNPK (15), YTIAALLSPYSYSTTAVVTNPKE (15)
HPP 50	14	14	AADDTWEPFASGK (8, 12), ALGISPFHEHAEVVFTANDSGPR (9-10, 12), GSPAINVAVHVFR (8-12), TSESGELHGLTTEEEFVEGIYK (9-12), YTIAALLSPYSYSTTAVVTNPK (9, 11, 12), YTIAALLSPYSYSTTAVVTNPKE (8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	14	15	AADDTWEPFASGK (9-14), ALGISPFHEHAEVVFTANDSGPR (11-14), GPTGTGESKCPLMVK (13), GSPAINVAVHVFR (10-12, 14, 15), GSPAINVAVHVFRK (13), KAADDTWEPFASGK (10, 12, 13, 14), RYTIAALLSPYSYSTTAVVTNPK (10, 12, 14), TSESGELHGLTTEEEFVEGIYK (8-16), VLDAVRGSPAINVAVHVFR (13), YTIAALLSPYSYSTTAVVTNPK (10-12, 14, 15), YTIAALLSPYSYSTTAVVTNPKE (9-10, 12, 14, 15)
HPP 50	14	16	AADDTWEPFASGK (7-11), ALGISPFHEHAEVVFTANDSGPR (7-12), CPLMVK (9), CPLMVKVLDAVR (11), GSPAINVAVHVFR (8-11), KAADDTWEPFASGK (9-10), RYTIAALLSPYSYSTTAVVTNPK (10), TSESGELHGLTTEEEFVEGIYK (8-13), YTIAALLSPYSYSTTAVVTNPK (8-11), YTIAALLSPYSYSTTAVVTNPKE (9, 11, 12)
HPP 50	14	17	AADDTWEPFASGK (8-11, 14, 15), ALGISPFHEHAEVVFTANDSGPR (9-11, 13), CPLMVK (9, 11, 12), GSPAINVAVHVFR (8-10, 12, 14), GSPAINVAVHVFRK (11), KAADDTWEPFASGK (11), RYTIAALLSPYSYSTTAVVTNPK (8, 12), TSESGELHGLTTEEEFVEGIYK (7-16), VLDAVRGSPAINVAVHVFR (7-9), YTIAALLSPYSYSTTAVVTNPK (8-11), YTIAALLSPYSYSTTAVVTNPKE (12)
HPP 50	14	18	AADDTWEPFASGK (6-10), ALGISPFHEHAEVVFTANDSGPR (6), GPTGTGESKCPLMVK (7), GSPAINVAVHVFR (6-8), KAADDTWEPFASGK (6-7), RYTIAALLSPYSYSTTAVVTNPK (8-9), TSESGELHGLTTEEEFVEGIYK (6-12, 14), YTIAALLSPYSYSTTAVVTNPK (6-9), YTIAALLSPYSYSTTAVVTNPKE (6-7)
HPP 50	14	19	AADDTWEPFASGK (6-8, 11, 12), ALGISPFHEHAEVVFTANDSGPR (6-8), CPLMVK (7), GPTGTGESKCPLMVK (7), GSPAINVAVHVFR (6-7), RYTIAALLSPYSYSTTAVVTNPK (7), TSESGELHGLTTEEEFVEGIYK (6-7, 9, 10, 11, 12, 13), YTIAALLSPYSYSTTAVVTNPK (6-7, 9, 12), YTIAALLSPYSYSTTAVVTNPKE (6-7, 12)
HPP 50	14	20	AADDTWEPFASGK (6-7), ALGISPFHEHAEVVFTANDSGPR (6, 10), GSPAINVAVHVFR (5-8), KAADDTWEPFASGK (6), TSESGELHGLTTEEEFVEGIYK (7-10, 12, 13), YTIAALLSPYSYSTTAVVTNPK (6, 9), YTIAALLSPYSYSTTAVVTNPKE (6)
HPP 50	14	21	AADDTWEPFASGK (5-6, 8), ALGISPFHEHAEVVFTANDSGPR (5-6), GSPAINVAVHVFR (5), TSESGELHGLTTEEEFVEGIYK (5-10, 13), YTIAALLSPYSYSTTAVVTNPK (6)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	14	22	AADDTWEPFASGK (4-5), GSPAINVAVHVFR (4-5), TSESGELHGLTTEEEFVEGIYK (5), YTIAALLSPYSYSTTAVVTNPK (5)
HPP 50	14	23	AADDTWEPFASGK (3-6), GSPAINVAVHVFR (3), KAADDTWEPFASGK (4), RYTIAALLSPYSYSTTAVVTNPK (4, 6), TSESGELHGLTTEEEFVEGIYK (4-8), VLDAVRGSPAINVAVHVFR (4)
HPP 50	14	24	AADDTWEPFASGK (3), ALGISPFHEHAEVVFTANDSGPR (1, 4), GSPAINVAVHVFR (1), TSESGELHGLTTEEEFVEGIYK (2-5), VLDAVRGSPAINVAVHVFR (3), YTIAALLSPYSYSTTAVVTNPK (2-3)
HPP 50	14	25	AADDTWEPFASGK (2-3), CPLMVK (2), RYTIAALLSPYSYSTTAVVTNPK (3), TSESGELHGLTTEEEFVEGIYK (1-7), YTIAALLSPYSYSTTAVVTNPK (3, 5)
HPP 50	14	26	AADDTWEPFASGK (2), GSPAINVAVHVFR (1), TSESGELHGLTTEEEFVEGIYK (1-5, 7), YTIAALLSPYSYSTTAVVTNPK (3)
HPP 50	14	27	TSESGELHGLTTEEEFVEGIYK (1-3)
HPP 50	14	28	AADDTWEPFASGK (4), ALGISPFHEHAEVVFTANDSGPR (4), RYTIAALLSPYSYSTTAVVTNPK (4), TSESGELHGLTTEEEFVEGIYK (4)
HPP 50	14	29	AADDTWEPFASGK (5), RYTIAALLSPYSYSTTAVVTNPK (4), TSESGELHGLTTEEEFVEGIYK (3-5)
HPP 50	14	30	AADDTWEPFASGK (4), ALGISPFHEHAEVVFTANDSGPR (3), RYTIAALLSPYSYSTTAVVTNPK (4), TSESGELHGLTTEEEFVEGIYK (3-5)
HPP 50	15	9	YTIAALLSPYSYSTTAVVTNPK (11), YTIAALLSPYSYSTTAVVTNPKE (11)
HPP 50	15	13	AADDTWEPFASGK (16-18), ALGISPFHEHAEVVFTANDSGPR (14, 16, 17, 18), ALGISPFHEHAEVVFTANDSGPRR (16-17), KAADDTWEPFASGK (15, 17), RYTIAALLSPYSYSTTAVVTNPK (14, 16), TSESGELHGLTTEEEFVEGIYK (12, 14, 15, 16, 18), YTIAALLSPYSYSTTAVVTNPK (16, 18), YTIAALLSPYSYSTTAVVTNPKE (16, 19)
HPP 50	15	14	AADDTWEPFASGK (12-13, 15), ALGISPFHEHAEVVFTANDSGPR (10-13, 15), GSPAINVAVHVFR (10, 13), KAADDTWEPFASGK (12-13, 15), RYTIAALLSPYSYSTTAVVTNPK (13, 15), TSESGELHGLTTEEEFVEGIYK (11-15), YTIAALLSPYSYSTTAVVTNPK (12-13, 15), YTIAALLSPYSYSTTAVVTNPKE (11-13, 15)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	15	15	AADDTWEPFASGK (10-17), ALGISPFHEHAEVVFTANDSGPR (11, 13, 14), CPLMVK (15), GSPAINVAVHVFR (10-12, 14, 16), GSPAINVAVHVFRK (13), KAADDTWEPFASGK (13, 15), RYTIAALLSPYSYSTTAVVTNPK (11, 15, 16), TSESGELHGLTTEEEFVEGIYK (10-19), YTIAALLSPYSYSTTAVVTNPK (14-15, 17), YTIAALLSPYSYSTTAVVTNPKE (16-17)
HPP 50	15	16	AADDTWEPFASGK (8-12), ALGISPFHEHAEVVFTANDSGPR (9), GSPAINVAVHVFR (8), KAADDTWEPFASGK (7), TSESGELHGLTTEEEFVEGIYK (7-10, 12, 13, 14, 15), YTIAALLSPYSYSTTAVVTNPK (8-10, 12), YTIAALLSPYSYSTTAVVTNPKE (11)
HPP 50	15	17	AADDTWEPFASGK (11, 13), GSPAINVAVHVFR (8, 10, 11, 12), KAADDTWEPFASGK (10-11), RYTIAALLSPYSYSTTAVVTNPK (9-11), TSESGELHGLTTEEEFVEGIYK (8, 10, 11, 14), YTIAALLSPYSYSTTAVVTNPK (9-12)
HPP 50	15	18	GSPAINVAVHVFR (7-9), TSESGELHGLTTEEEFVEGIYK (6-7), YTIAALLSPYSYSTTAVVTNPK (7-8)
HPP 50	15	19	AADDTWEPFASGK (7), GSPAINVAVHVFR (11), TSESGELHGLTTEEEFVEGIYK (8, 10, 11)
HPP 50	15	20	AADDTWEPFASGK (5), TSESGELHGLTTEEEFVEGIYK (5), YTIAALLSPYSYSTTAVVTNPK (5)
HPP 50	15	21	AADDTWEPFASGK (4), RYTIAALLSPYSYSTTAVVTNPK (6), TSESGELHGLTTEEEFVEGIYK (7), YTIAALLSPYSYSTTAVVTNPK (5), YTIAALLSPYSYSTTAVVTNPKE (6)
HPP 50	15	22	AADDTWEPFASGK (4), TSESGELHGLTTEEEFVEGIYK (3-4, 6, 7, 8), YTIAALLSPYSYSTTAVVTNPKE (4)
HPP 50	15	23	TSESGELHGLTTEEEFVEGIYK (3-5)
HPP 50	15	24	AADDTWEPFASGK (2), TSESGELHGLTTEEEFVEGIYK (2-6, 8)
HPP 50	15	25	AADDTWEPFASGK (3), TSESGELHGLTTEEEFVEGIYK (3-4)
HPP 50	15	26	AADDTWEPFASGK (1-3), TSESGELHGLTTEEEFVEGIYK (1-3), YTIAALLSPYSYSTTAVVTNPK (3)
HPP 50	15	27	TSESGELHGLTTEEEFVEGIYK (3), YTIAALLSPYSYSTTAVVTNPK (3), YTIAALLSPYSYSTTAVVTNPKE (3)
HPP 50	15	29	TSESGELHGLTTEEEFVEGIYK (3)
HPP 50	16	9	YTIAALLSPYSYSTTAVVTNPK (10)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	16	12	AADDTWEPFASGK (8), ALGISPFHEHAEVVFTANDSGPR (9), GSPAINVAVHVFR (8), RYTIAALLSPYSYSTTAVVTNPK (7), YTIAALLSPYSYSTTAVVTNPK (7-9, 11), YTIAALLSPYSYSTTAVVTNPKE (8)
HPP 50	16	14	AADDTWEPFASGK (17), ALGISPFHEHAEVVFTANDSGPR (17), GSPAINVAVHVFR (11, 13), TSESGELHGLTTEEEFVEGIYK (10-11, 17, 18), YTIAALLSPYSYSTTAVVTNPK (11-12)
HPP 50	16	15	AADDTWEPFASGK (15-20), ALGISPFHEHAEVVFTANDSGPR (16-18), ALGISPFHEHAEVVFTANDSGPRR (16), GSPAINVAVHVFR (16-17), KAADDTWEPFASGK (16), RYTIAALLSPYSYSTTAVVTNPK (10-11, 16, 17), TSESGELHGLTTEEEFVEGIYK (10, 12, 13, 14, 15, 16, 17, 18, 19, 22), YTIAALLSPYSYSTTAVVTNPK (10-12, 16, 17, 18), YTIAALLSPYSYSTTAVVTNPKE (16-17)
HPP 50	16	16	AADDTWEPFASGK (9), GSPAINVAVHVFR (9), RYTIAALLSPYSYSTTAVVTNPK (9), TSESGELHGLTTEEEFVEGIYK (7-10), YTIAALLSPYSYSTTAVVTNPK (9)
HPP 50	16	17	AADDTWEPFASGK (7-11, 14, 16, 17, 18, 19), ALGISPFHEHAEVVFTANDSGPR (9-11, 18), CPLMVKVLDAVR (11, 19), GSPAINVAVHVFR (7, 10, 11, 13, 17, 18, 19), KAADDTWEPFASGK (10-11), RYTIAALLSPYSYSTTAVVTNPK (7-8, 11, 16, 17, 18), TSESGELHGLTTEEEFVEGIYK (7-21), YTIAALLSPYSYSTTAVVTNPK (7-12, 16, 18), YTIAALLSPYSYSTTAVVTNPKE (11, 18)
HPP 50	16	18	AADDTWEPFASGK (5-9), ALGISPFHEHAEVVFTANDSGPR (6-8), GSPAINVAVHVFR (7), KAADDTWEPFASGK (7), RYTIAALLSPYSYSTTAVVTNPK (6), TSESGELHGLTTEEEFVEGIYK (5-8, 10, 11), YTIAALLSPYSYSTTAVVTNPK (5-8), YTIAALLSPYSYSTTAVVTNPKE (6)
HPP 50	16	19	AADDTWEPFASGK (5), TSESGELHGLTTEEEFVEGIYK (5-7, 9, 10), YTIAALLSPYSYSTTAVVTNPK (5), YTIAALLSPYSYSTTAVVTNPKE (5-7)
HPP 50	16	20	AADDTWEPFASGK (6, 8), GSPAINVAVHVFR (4), TSESGELHGLTTEEEFVEGIYK (3-11), YTIAALLSPYSYSTTAVVTNPKE (5)
HPP 50	16	21	AADDTWEPFASGK (5-7), ALGISPFHEHAEVVFTANDSGPR (5), GSPAINVAVHVFR (5-6), RYTIAALLSPYSYSTTAVVTNPK (5-6), TSESGELHGLTTEEEFVEGIYK (4-8), YTIAALLSPYSYSTTAVVTNPK (4-6), YTIAALLSPYSYSTTAVVTNPKE (5)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	16	22	AADDTWEPFASGK (2-5), GSPAINVAVHVFR (4, 6), RYTIAALLSPYSYSTTAVVTNPK (4), TSESGELHGLTTEEEFVEGIYK (3-7), YTIAALLSPYSYSTTAVVTNPK (2-4), YTIAALLSPYSYSTTAVVTNPKE (4-5)
HPP 50	16	23	AADDTWEPFASGK (2-4), GSPAINVAVHVFR (2-4), TSESGELHGLTTEEEFVEGIYK (2-4), YTIAALLSPYSYSTTAVVTNPK (2)
HPP 50	16	24	AADDTWEPFASGK (1-4), CPLMVK (2), GSPAINVAVHVFR (1-3), TSESGELHGLTTEEEFVEGIYK (1-5), YTIAALLSPYSYSTTAVVTNPK (2)
HPP 50	16	25	AADDTWEPFASGK (2-3), GSPAINVAVHVFR (2), TSESGELHGLTTEEEFVEGIYK (1-3, 5, 6), YTIAALLSPYSYSTTAVVTNPK (2-3)
HPP 50	16	26	AADDTWEPFASGK (2-3), GSPAINVAVHVFR (2-3), TSESGELHGLTTEEEFVEGIYK (2-4, 7, 9)
HPP 50	16	27	AADDTWEPFASGK (2-4, 7), GSPAINVAVHVFR (4), TSESGELHGLTTEEEFVEGIYK (3-6), YTIAALLSPYSYSTTAVVTNPK (3)
HPP 50	16	28	AADDTWEPFASGK (2-4), GSPAINVAVHVFR (3-4), TSESGELHGLTTEEEFVEGIYK (2-5, 7), YTIAALLSPYSYSTTAVVTNPK (4)
HPP 50	16	29	AADDTWEPFASGK (2-4), GSPAINVAVHVFR (3), TSESGELHGLTTEEEFVEGIYK (2-5)
HPP 50	16	30	AADDTWEPFASGK (2-4), TSESGELHGLTTEEEFVEGIYK (2-5), YTIAALLSPYSYSTTAVVTNPK (4)
HPP 50	17	10	RYTIAALLSPYSYSTTAVVTNPK (8), YTIAALLSPYSYSTTAVVTNPK (8)
HPP 50	17	14	TSESGELHGLTTEEEFVEGIYK (9-10)
HPP 50	17	15	AADDTWEPFASGK (9-11), ALGISPFHEHAEVVFTANDSGPR (9, 11, 13), CPLMVK (12), GSPAINVAVHVFR (9, 11, 12), GSPAINVAVHVFRK (9-10), RYTIAALLSPYSYSTTAVVTNPK (11-12), TSESGELHGLTTEEEFVEGIYK (8-14), TSESGELHGLTTEEEFVEGIYKVEIDTK (10), YTIAALLSPYSYSTTAVVTNPK (11), YTIAALLSPYSYSTTAVVTNPKE (12-13)
HPP 50	17	16	AADDTWEPFASGK (7-9), ALGISPFHEHAEVVFTANDSGPR (8-9), ALGISPFHEHAEVVFTANDSGPRR (8-9), GPTGTGESKCPLMVK (9), GSPAINVAVHVFR (8-9), GSPAINVAVHVFRK (8-9), KAADDTWEPFASGK (9), RYTIAALLSPYSYSTTAVVTNPK (8), TSESGELHGLTTEEEFVEGIYK (7-10, 12), TSESGELHGLTTEEEFVEGIYKVEIDTK (7), YTIAALLSPYSYSTTAVVTNPK (8-9), YTIAALLSPYSYSTTAVVTNPKE (7-9)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	17	17	AADDTWEPFASGK (7-12), ALGISPFHEHAEVVFTANDSGPR (7-10), ALGISPFHEHAEVVFTANDSGPRR (9), CPLMVK (9-10), CPLMVKVLDAVR (11), GPTGTGESKCPLMVK (9), GSPAINVAVHVFR (8-10), KAADDTWEPFASGK (7, 9), RYTIAALLSPYSYSTTAVVTNPK (7-10), TSESGELHGLTTEEEFVEGIYK (7-14), TSESGELHGLTTEEEFVEGIYKVEIDTK (11), VLDAVRGSPAINVAVHVFR (9), YTIAALLSPYSYSTTAVVTNPK (7-12), YTIAALLSPYSYSTTAVVTNPKE (8-12)
HPP 50	17	18	AADDTWEPFASGK (6-8), ALGISPFHEHAEVVFTANDSGPR (6-8, 10), GSPAINVAVHVFR (6-8), KAADDTWEPFASGK (6-7), RYTIAALLSPYSYSTTAVVTNPK (6-7), TSESGELHGLTTEEEFVEGIYK (6-9, 11), VLDAVRGSPAINVAVHVFR (6), YTIAALLSPYSYSTTAVVTNPK (5-9), YTIAALLSPYSYSTTAVVTNPKE (5, 7)
HPP 50	17	19	AADDTWEPFASGK (6-7), ALGISPFHEHAEVVFTANDSGPR (7-8), GSPAINVAVHVFR (7), KAADDTWEPFASGK (6-8), RYTIAALLSPYSYSTTAVVTNPK (7), TSESGELHGLTTEEEFVEGIYK (5-8), YTIAALLSPYSYSTTAVVTNPK (6-8), YTIAALLSPYSYSTTAVVTNPKE (6-7)
HPP 50	17	20	AADDTWEPFASGK (5-6, 9), GPTGTGESKCPLMVK (6), GSPAINVAVHVFR (5-6), GSPAINVAVHVFRK (6), KAADDTWEPFASGK (5-6), TSESGELHGLTTEEEFVEGIYK (5, 8, 9, 10, 12), YTIAALLSPYSYSTTAVVTNPKE (5-6)
HPP 50	17	21	AADDTWEPFASGK (5-8), ALGISPFHEHAEVVFTANDSGPR (7), GSPAINVAVHVFR (5), RYTIAALLSPYSYSTTAVVTNPK (5), TSESGELHGLTTEEEFVEGIYK (4-9, 12), YTIAALLSPYSYSTTAVVTNPK (4-6, 8)
HPP 50	17	22	AADDTWEPFASGK (3-6), ALGISPFHEHAEVVFTANDSGPR (4, 6), GSPAINVAVHVFR (3-4), KAADDTWEPFASGK (4), RYTIAALLSPYSYSTTAVVTNPK (4), TSESGELHGLTTEEEFVEGIYK (3-5, 7), YTIAALLSPYSYSTTAVVTNPK (3-6)
HPP 50	17	23	AADDTWEPFASGK (4, 6), ALGISPFHEHAEVVFTANDSGPR (5-6), KAADDTWEPFASGK (3-4), RYTIAALLSPYSYSTTAVVTNPK (4), TSESGELHGLTTEEEFVEGIYK (3-9), YTIAALLSPYSYSTTAVVTNPK (3-6), YTIAALLSPYSYSTTAVVTNPKE (4)
HPP 50	17	24	AADDTWEPFASGK (2, 4), ALGISPFHEHAEVVFTANDSGPR (2-3), GSPAINVAVHVFR (1-3), GSPAINVAVHVFRK (2), TSESGELHGLTTEEEFVEGIYK (1-5), YTIAALLSPYSYSTTAVVTNPK (2-3)

Table 3			
Protein	**CEX**	**RP1**	**Tryptic Sequence (RP2 fractions)**
HPP 50	17	25	AADDTWEPFASGK (3-4), ALGISPFHEHAEVVFTANDSGPR (4), GSPAINVAVHVFR (1-4), GSPAINVAVHVFRK (4), KAADDTWEPFASGK (4), RYTIAALLSPYSYSTTAVVTNPK (3), TSESGELHGLTTEEEFVEGIYK (1, 3, 4, 5, 7), TSESGELHGLTTEEEFVEGIYKVEIDTK (2), YTIAALLSPYSYSTTAVVTNPK (1, 3, 4), YTIAALLSPYSYSTTAVVTNPKE (2)
HPP 50	17	26	AADDTWEPFASGK (1, 4), GSPAINVAVHVFR (4), RYTIAALLSPYSYSTTAVVTNPK (2), TSESGELHGLTTEEEFVEGIYK (1-5, 8), YTIAALLSPYSYSTTAVVTNPK (1), YTIAALLSPYSYSTTAVVTNPKE (4)
HPP 50	17	27	AADDTWEPFASGK (4-5), ALGISPFHEHAEVVFTANDSGPR (3-4), GSPAINVAVHVFR (3-5), RYTIAALLSPYSYSTTAVVTNPK (4), TSESGELHGLTTEEEFVEGIYK (2-7), YTIAALLSPYSYSTTAVVTNPK (3-4)
HPP 50	17	28	AADDTWEPFASGK (3-4), GSPAINVAVHVFR (3-4), KAADDTWEPFASGK (3-4), RYTIAALLSPYSYSTTAVVTNPK (4), TSESGELHGLTTEEEFVEGIYK (2-7), YTIAALLSPYSYSTTAVVTNPK (3-4), YTIAALLSPYSYSTTAVVTNPKE (3)
HPP 50	17	29	AADDTWEPFASGK (4), ALGISPFHEHAEVVFTANDSGPR (3-4), GSPAINVAVHVFR (3-4), RYTIAALLSPYSYSTTAVVTNPK (4), TSESGELHGLTTEEEFVEGIYK (2-8), YTIAALLSPYSYSTTAVVTNPK (3-4)
HPP 50	17	30	AADDTWEPFASGK (3-4, 7), ALGISPFHEHAEVVFTANDSGPR (4), GSPAINVAVHVFR (3), KAADDTWEPFASGK (4), RYTIAALLSPYSYSTTAVVTNPK (3-4), TSESGELHGLTTEEEFVEGIYK (2-6), YTIAALLSPYSYSTTAVVTNPK (3-4), YTIAALLSPYSYSTTAVVTNPKE (3-4)
HPP 50	18	13	TSESGELHGLTTEEEFVEGIYK (10)
HPP 50	18	15	AADDTWEPFASGK (10), ALGISPFHEHAEVVFTANDSGPR (10), GSPAINVAVHVFR (9-10), KAADDTWEPFASGK (10), RYTIAALLSPYSYSTTAVVTNPK (11), TSESGELHGLTTEEEFVEGIYK (9-11, 13), YTIAALLSPYSYSTTAVVTNPK (10)
HPP 50	18	16	AADDTWEPFASGK (7-8), ALGISPFHEHAEVVFTANDSGPR (7-9), CPLMVK (8), GSPAINVAVHVFR (7-9), GSPAINVAVHVFRK (7), KAADDTWEPFASGK (7-8), RYTIAALLSPYSYSTTAVVTNPK (8-9), TSESGELHGLTTEEEFVEGIYK (7-10), VLDAVR (8), VLDAVRGSPAINVAVHVFR (8), YTIAALLSPYSYSTTAVVTNPK (7-9), YTIAALLSPYSYSTTAVVTNPKE (7-8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	18	17	AADDTWEPFASGK (7-12), ALGISPFHEHAEVVFTANDSGPR (7-9, 12), CPLMVK (9), GSPAINVAVHVFR (7-10, 12), GSPAINVAVHVFRK (7, 9), KAADDTWEPFASGK (8-10), RYTIAALLSPYSYSTTAVVTNPK (8-9), TSESGELHGLTTEEEFVEGIYK (7-12), TSESGELHGLTTEEEFVEGIYKVEIDTK (9), YTIAALLSPYSYSTTAVVTNPK (7-12), YTIAALLSPYSYSTTAVVTNPKE (7, 9, 10, 11, 12)
HPP 50	18	18	AADDTWEPFASGK (5-11), ALGISPFHEHAEVVFTANDSGPR (5-11), GSPAINVAVHVFR (5-11), KAADDTWEPFASGK (6, 9), RYTIAALLSPYSYSTTAVVTNPK (5-7, 9), TSESGELHGLTTEEEFVEGIYK (5-9, 11), YTIAALLSPYSYSTTAVVTNPK (5-9), YTIAALLSPYSYSTTAVVTNPKE (6, 9)
HPP 50	18	19	AADDTWEPFASGK (5-7, 9, 10, 11, 14), ALGISPFHEHAEVVFTANDSGPR (6-9, 11), ALGISPFHEHAEVVFTANDSGPRR (7), GPTGTGESKCPLMVK (7-8), GSPAINVAVHVFR (6, 9, 10), GSPAINVAVHVFRK (7, 9, 10), KAADDTWEPFASGK (6-7), RYTIAALLSPYSYSTTAVVTNPK (7, 10, 11), TSESGELHGLTTEEEFVEGIYK (6-8, 11, 12, 13), VLDAVRGSPAINVAVHVFR (8), YTIAALLSPYSYSTTAVVTNPK (6, 10, 11), YTIAALLSPYSYSTTAVVTNPKE (5, 9, 11)
HPP 50	18	20	AADDTWEPFASGK (4-8), ALGISPFHEHAEVVFTANDSGPR (4-7, 9), ALGISPFHEHAEVVFTANDSGPRR (5-7), CPLMVK (5), GPTGTGESKCPLMVK (6), GSPAINVAVHVFR (4-8), GSPAINVAVHVFRK (5, 7, 8), KAADDTWEPFASGK (5), TSESGELHGLTTEEEFVEGIYK (4-6, 8, 9, 12), YTIAALLSPYSYSTTAVVTNPK (4-5, 9), YTIAALLSPYSYSTTAVVTNPKE (4-6, 8, 10)
HPP 50	18	21	AADDTWEPFASGK (4-8), ALGISPFHEHAEVVFTANDSGPR (5, 8), GSPAINVAVHVFR (5-8), KAADDTWEPFASGK (6), RYTIAALLSPYSYSTTAVVTNPK (5-7), TSESGELHGLTTEEEFVEGIYK (4-11), YTIAALLSPYSYSTTAVVTNPK (4-9), YTIAALLSPYSYSTTAVVTNPKE (5)
HPP 50	18	22	AADDTWEPFASGK (3-6), ALGISPFHEHAEVVFTANDSGPR (4), CPLMVK (6), GSPAINVAVHVFR (3-7), GSPAINVAVHVFRK (3-4), KAADDTWEPFASGK (3-4), RYTIAALLSPYSYSTTAVVTNPK (4-5), TSESGELHGLTTEEEFVEGIYK (4-6), YTIAALLSPYSYSTTAVVTNPK (4-6), YTIAALLSPYSYSTTAVVTNPKE (3-5)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	18	23	AADDTWEPFASGK (3-6), ALGISPFHEHAEVVFTANDSGPR (3-7), ALGISPFHEHAEVVFTANDSGPRR (4), GPTGTGESKCPLMVK (4), GSPAINVAVHVFR (3-7), GSPAINVAVHVFRK (4), KAADDTWEPFASGK (6), RYTIAALLSPYSYSTTAVVTNPK (3, 5, 6), TSESGELHGLTTEEEFVEGIYK (3-10), YTIAALLSPYSYSTTAVVTNPK (3-5, 7), YTIAALLSPYSYSTTAVVTNPKE (4)
HPP 50	18	24	AADDTWEPFASGK (1-6), ALGISPFHEHAEVVFTANDSGPR (1-2), GPTGTGESKCPLMVK (2), GSPAINVAVHVFR (1-6), GSPAINVAVHVFRK (2), TSESGELHGLTTEEEFVEGIYK (1-8), YTIAALLSPYSYSTTAVVTNPK (1-2, 5), YTIAALLSPYSYSTTAVVTNPKE (2)
HPP 50	18	25	AADDTWEPFASGK (1-2, 4, 8), ALGISPFHEHAEVVFTANDSGPR (1-3), ALGISPFHEHAEVVFTANDSGPRR (2), GPTGTGESKCPLMVK (4), GSPAINVAVHVFR (2-5), GSPAINVAVHVFRK (2), KAADDTWEPFASGK (2-3), TSESGELHGLTTEEEFVEGIYK (1-5), YTIAALLSPYSYSTTAVVTNPK (3, 8), YTIAALLSPYSYSTTAVVTNPKE (1, 3)
HPP 50	18	26	AADDTWEPFASGK (3-8), ALGISPFHEHAEVVFTANDSGPR (3-4), ALGISPFHEHAEVVFTANDSGPRR (4), GPTGTGESKCPLMVK (4-5), GSPAINVAVHVFR (3-5), GSPAINVAVHVFRK (3-6), KAADDTWEPFASGK (3-5), TSESGELHGLTTEEEFVEGIYK (3-4, 6, 8), TSESGELHGLTTEEEFVEGIYKVEIDTK (4), YTIAALLSPYSYSTTAVVTNPK (5, 8), YTIAALLSPYSYSTTAVVTNPKE (3-6)
HPP 50	18	27	AADDTWEPFASGK (3-6, 8), ALGISPFHEHAEVVFTANDSGPR (4), GSPAINVAVHVFR (3-5), KAADDTWEPFASGK (4-5), RYTIAALLSPYSYSTTAVVTNPK (4-5), TSESGELHGLTTEEEFVEGIYK (3-10), YTIAALLSPYSYSTTAVVTNPK (3-4, 6)
HPP 50	18	28	AADDTWEPFASGK (3-6, 8), ALGISPFHEHAEVVFTANDSGPR (4-5), CPLMVK (4), GPTGTGESKCPLMVK (4), GSPAINVAVHVFR (2, 4, 6), RYTIAALLSPYSYSTTAVVTNPK (4), TSESGELHGLTTEEEFVEGIYK (3-6, 8, 9), YTIAALLSPYSYSTTAVVTNPK (2, 4, 6)
HPP 50	18	29	AADDTWEPFASGK (3-6), ALGISPFHEHAEVVFTANDSGPR (3, 6), ALGISPFHEHAEVVFTANDSGPRR (4), GPTGTGESKCPLMVK (4), GSPAINVAVHVFR (2-4), KAADDTWEPFASGK (3-5), RYTIAALLSPYSYSTTAVVTNPK (3), TSESGELHGLTTEEEFVEGIYK (2-7), YTIAALLSPYSYSTTAVVTNPK (3, 6), YTIAALLSPYSYSTTAVVTNPKE (3-5, 7)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 50	18	30	AADDTWEPFASGK (2-6, 9), GPTGTGESKCPLMVK (4), GSPAINVAVHVFR (3-5), GSPAINVAVHVFRK (3-4), KAADDTWEPFASGK (4), TSESGELHGLTTEEEFVEGIYK (2, 5, 7, 8, 9), TSESGELHGLTTEEEFVEGIYKVEIDTK (3-4), YTIAALLSPYSYSTTAVVTNPK (5), YTIAALLSPYSYSTTAVVTNPKE (2-4)
HPP 51	1	7	GGSTSYGTGSETESPR (9), NPSSAGSWNSGSSGPGSTGNR (9)
HPP 51	2	3	ADSGEGDFLAEGGGVRGPR (16-17)
HPP 51	2	4	ADSGEGDFLAEGGGVRGPR (9), QFTSSTSYNRGDSTFESK (9)
HPP 51	3	4	ADSGEGDFLAEGGGVRGPR (8)
HPP 51	3	12	ESSSHHPGIAEFPSR (7), GSESGIFTNTK (7), QFTSSTSYNR (7), TFPGFFSPMLGEFVSETESR (7)
HPP 51	4	12	ESSSHHPGIAEFPSR (6-7), ESSSHHPGIAEFPSRGK (7), GSESGIFTNTK (6-7), GSESGIFTNTKESSSHHPGIAEFPSR (7), QFTSSTSYNRGDSTFESK (6-7), TFPGFFSPMLGEFVSETESR (7-8)
HPP 51	5	7	ADSGEGDFLAEGGGVR (10-11), ADSGEGDFLAEGGGVRGPR (10-12), GSESGIFTNTK (11)
HPP 51	6	8	ADSGEGDFLAEGGGVR (8), ESSSHHPGIAEFPSR (7), GGSTSYGTGSETESPR (8), QFTSSTSYNRGDSTFESK (7)
HPP 51	6	10	ESSSHHPGIAEFPSR (7-8), GSESGIFTNTK (4-5, 7, 8), HRHPDEAAFFDTASTGK (8), QFTSSTSYNR (7-8), TFPGFFSPMLGEFVSETESR (7-8)
HPP 51	6	12	ESSSHHPGIAEFPSR (6-7), QFTSSTSYNR (7), QFTSSTSYNRGDSTFESK (6-7), TFPGFFSPMLGEFVSETESR (7, 9)
HPP 51	6	13	GSESGIFTNTK (8), TFPGFFSPMLGEFVSETESR (8)
HPP 51	7	8	ESSSHHPGIAEFPSR (8-9), GSESGIFTNTK (8-9), QFTSSTSYNR (8), QFTSSTSYNRGDSTFESK (6, 8)
HPP 51	7	9	ESSSHHPGIAEFPSR (8-9), GSESGIFTNTK (8), TFPGFFSPMLGEFVSETESR (9)
HPP 51	7	10	ESSSHHPGIAEFPSR (7-9), GSESGIFTNTK (8-9), HRHPDEAAFFDTASTGK (9, 11), QFTSSTSYNR (8), QFTSSTSYNRGDSTFESK (8), TFPGFFSPMLGEFVSETESR (8-9)
HPP 51	7	11	ESSSHHPGIAEFPSR (7-10), GSESGIFTNTK (7-10), HRHPDEAAFFDTASTGK (12), TFPGFFSPMLGEFVSETESR (9-10)
HPP 51	8	4	ESSSHHPGIAEFPSR (12), QFTSSTSYNR (12)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 51	8	11	ESSSHHPGIAEFPSR (8), GSESGIFTNTK (9), HRHPDEAAFFDTASTGK (8-9), QLEQVIAK (12)
HPP 51	8	12	ESSSHHPGIAEFPSR (5-6), GSESGIFTNTK (5), QFTSSTSYNR (5), QLEQVIAK (7), TFPGFFSPMLGEFVSETESR (6)
HPP 51	8	13	ESSSHHPGIAEFPSR (6-8), HPDEAAFFDTASTGK (8), HRHPDEAAFFDTASTGK (7-9), TFPGFFSPMLGEFVSETESR (6-8)
HPP 51	9	11	ADSGEGDFLAEGGGVR (10), HPDEAAFFDTASTGK (10), MKPVPDLVPGNFK (16), QFTSSTSYNR (9-10), TFPGFFSPMLGEFVSETESR (9)
HPP 51	9	12	ESSSHHPGIAEFPSR (7-8), TFPGFFSPMLGEFVSETESR (7-8)
HPP 51	10	8	EVVTSEDGSDCPEAMDLGTLSGIGTLDGFR (9-10)
HPP 51	10	9	GGSTSYGTGSETESPR (15), HRHPDEAAFFDTASTGK (14-15), QFTSSTSYNR (14-15)
HPP 51	10	11	ESSSHHPGIAEFPSR (8), HPDEAAFFDTASTGK (8), HRHPDEAAFFDTASTGK (8-9), TFPGFFSPMLGEFVSETESR (8-9)
HPP 51	10	13	HRHPDEAAFFDTASTGK (7-8), TFPGFFSPMLGEFVSETESR (7)
HPP 51	11	8	EVVTSEDGSDCPEAMDLGTLSGIGTLDGFR (7), GSESGIFTNTK (7)
HPP 51	11	11	ESSSHHPGIAEFPSR (9), GSESGIFTNTK (9), HRHPDEAAFFDTASTGK (9), TFPGFFSPMLGEFVSETESR (9)
HPP 51	13	8	EVVTSEDGSDCPEAMDLGTLSGIGTLDGFR (8)
HPP 51	13	10	EVVTSEDGSDCPEAMDLGTLSGIGTLDGFR (7)
HPP 51	13	12	ESSSHHPGIAEFPSR (8), TFPGFFSPMLGEFVSETESR (8)
HPP 51	14	9	ESSSHHPGIAEFPSR (8), GSESGIFTNTK (8), TFPGFFSPMLGEFVSETESR (9)
HPP 51	14	10	ESSSHHPGIAEFPSR (9), EVVTSEDGSDCPEAMDLGTLSGIGTLDGFR (8), GSESGIFTNTK (9), HPDEAAFFDTASTGK (8-9), TFPGFFSPMLGEFVSETESR (8-9)
HPP 51	14	11	ESSSHHPGIAEFPSR (7)
HPP 51	15	10	ESSSHHPGIAEFPSR (7-8), EVVTSEDGSDCPEAMDLGTLSGIGTLDGFR (7-8), GSESGIFTNTK (7), HPDEAAFFDTASTGK (8), HRHPDEAAFFDTASTGK (8), TFPGFFSPMLGEFVSETESR (8)
HPP 51	15	11	ESSSHHPGIAEFPSR (8-9), GSESGIFTNTK (7, 9, 10), HPDEAAFFDTASTGK (8-9), HRHPDEAAFFDTASTGK (8), QFTSSTSYNR (7, 10), QFTSSTSYNRGDSTFESK (8), TFPGFFSPMLGEFVSETESR (8-12)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 51	15	12	ESSSHHPGIAEFPSR (7-8), EVVTSEDGSDCPEAMDLGTLSGIGTLDGFR (7-8), GSESGIFTNTK (7), HPDEAAFFDTASTGK (7), QFTSSTSYNR (6-7), TFPGFFSPMLGEFVSETESR (6-8, 10)
HPP 51	15	13	ESSSHHPGIAEFPSR (7-8), EVVTSEDGSDCPEAMDLGTLSGIGTLDGFR (9), HPDEAAFFDTASTGK (8-9), HRHPDEAAFFDTASTGK (8-9), QFTSSTSYNRGDSTFESK (7), TFPGFFSPMLGEFVSETESR (8-9)
HPP 51	16	12	ESSSHHPGIAEFPSR (6-8), GSESGIFTNTK (7-8), QFTSSTSYNR (7), TFPGFFSPMLGEFVSETESR (7-8)
HPP 51	16	13	ESSSHHPGIAEFPSR (6-7), HPDEAAFFDTASTGK (6-7), HRHPDEAAFFDTASTGK (6-7), TFPGFFSPMLGEFVSETESR (6-7)
HPP 51	16	14	ESSSHHPGIAEFPSR (6), GSESGIFTNTK (1, 6), QFTSSTSYNR (6)
HPP 51	16	20	TFPGFFSPMLGEFVSETESR (1)
HPP 51	17	14	ADSGEGDFLAEGGGVR (9, 11), ALTDMPQMR (9), ESSSHHPGIAEFPSR (5-6), GGSTSYGTGSETESPR (11), GLIDEVNQDFTNR (9), HRHPDEAAFFDTASTGK (5), MELERPGGNEITR (9), MKPVPDLVPGNFK (9), NSLFEYQK (9), QFTSSTSYNR (9), QLEQVIAK (9, 11), TFPGFFSPMLGEFVSETESR (6, 8, 9), VQHIQLLQK (9)
HPP 51	17	15	ADSGEGDFLAEGGGVR (9, 11, 12, 13, 14), ADSGEGDFLAEGGGVRGPR (10), ALTDMPQMR (12), DSDWPFCSDEDWNYK (12), DSHSLTTNIMEILR (9-14), ESSSHHPGIAEFPSR (9), EVDLKDYEDQQK (13), GDFSSANNRDNTYNR (10), GGSTSYGTGSETESPR (13), GLIDEVNQDFTNR (9, 11, 12, 13, 14), HRHPDEAAFFDTASTGK (10, 13, 14), MELERPGGNEITR (13), NPSSAGSWNSGSSGPGSTGNR (9, 11), NSLFEYQK (9, 12), QFTSSTSYNR (12), QFTSSTSYNRGDSTFESK (10), QLEQVIAK (9, 13, 14), TFPGFFSPMLGEFVSETESR (9-13), VQHIQLLQK (9, 13)
HPP 51	17	16	ADSGEGDFLAEGGGVR (7, 9), GLIDEVNQDFTNR (7), NSLFEYQK (9)
HPP 51	17	17	ADSGEGDFLAEGGGVR (8-12), ESSSHHPGIAEFPSR (9, 12), GLIDEVNQDFTNR (8-12), HRHPDEAAFFDTASTGK (9, 11, 12), NPSSAGSWNSGSSGPGSTGNR (8, 10)
HPP 51	17	18	ADSGEGDFLAEGGGVR (6), GLIDEVNQDFTNR (6)
HPP 51	17	19	ADSGEGDFLAEGGGVRGPR (6), DSHSLTTNIMEILR (6)
HPP 51	17	20	ADSGEGDFLAEGGGVRGPR (4), HRHPDEAAFFDTASTGK (4), NSLFEYQK (4), TFPGFFSPMLGEFVSETESR (4)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 51	17	21	ADSGEGDFLAEGGGVR (4), GLIDEVNQDFTNR (5), NSLFEYQK (4), TFPGFFSPMLGEFVSETESR (4), VQHIQLLQK (4)
HPP 51	17	22	ADSGEGDFLAEGGGVR (3), DSHSLTTNIMEILR (3), GLIDEVNQDFTNR (3), QFTSSTSYNRGDSTFESK (2), QLEQVIAK (3), TFPGFFSPMLGEFVSETESR (2-3), VQHIQLLQK (3)
HPP 51	17	23	ADSGEGDFLAEGGGVR (3), DCDDVLQTHPSGTQSGIFNIK (2), DSDWPFCSDEDWNYK (3), GLIDEVNQDFTNR (3), NPSSAGSWNSGSSGPGSTGNR (3), QFTSSTSYNR (2-3), TFPGFFSPMLGEFVSETESR (3)
HPP 51	17	24	ADSGEGDFLAEGGGVRGPR (1)
HPP 51	17	25	ADSGEGDFLAEGGGVRGPR (1), DLLPSRDR (1), HRHPDEAAFFDTASTGK (1), TFPGFFSPMLGEFVSETESR (1)
HPP 51	17	26	ADSGEGDFLAEGGGVRGPR (2-3), GDFSSANNRDNTYNR (2), NNKDSHSLTTNIMEILR (3), TFPGFFSPMLGEFVSETESR (3)
HPP 51	17	27	ADSGEGDFLAEGGGVR (3), DSHSLTTNIMEILR (3), GLIDEVNQDFTNR (2-5), MKPVPDLVPGNFK (3), QLEQVIAK (3), TFPGFFSPMLGEFVSETESR (3), VQHIQLLQK (3)
HPP 51	17	28	ADSGEGDFLAEGGGVR (2), GLIDEVNQDFTNR (3), NPSSAGSWNSGSSGPGSTGNR (2-3), TFPGFFSPMLGEFVSETESR (3), VQHIQLLQK (4)
HPP 51	17	29	ADSGEGDFLAEGGGVR (2-3), DSDWPFCSDEDWNYK (3), DSHSLTTNIMEILR (3), EVVTSEDGSDCPEAMDLGTLSGIGTLDGFR (2), GGSTSYGTGSETESPR (2), GLIDEVNQDFTNR (3), HPDEAAFFDTASTGK (3), NPSSAGSWNSGSSGPGSTGNR (2-3), TFPGFFSPMLGEFVSETESR (2-3)
HPP 51	17	30	ADSGEGDFLAEGGGVR (2, 5), DSDWPFCSDEDWNYK (2), GGSTSYGTGSETESPR (2-3), GLIDEVNQDFTNR (3), QFTSSTSYNR (2), TFPGFFSPMLGEFVSETESR (2-3), VQHIQLLQK (3)
HPP 51	18	17	ADSGEGDFLAEGGGVR (12-13), ESSSHHPGIAEFPSR (12-13), EVDLKDYEDQQK (12), HRHPDEAAFFDTASTGK (12-13), MELERPGGNEITR (12), QFTSSTSYNR (12-13), QLEQVIAK (12-13), TFPGFFSPMLGEFVSETESR (6, 12)
HPP 51	18	18	GLIDEVNQDFTNR (5)
HPP 51	18	19	ADSGEGDFLAEGGGVR (5), EVVTSEDGSDCPEAMDLGTLSGIGTLDGFR (5)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 51	18	29	NNKDSHSLTTNIMEILR (2), TFPGFFSPMLGEFVSETESR (2)
HPP 51	18	30	TFPGFFSPMLGEFVSETESR (4)
HPP 52	4	23	TPHVLTHR (5)
HPP 52	9	12	TPHVLTHR (18)
HPP 53	3	6	SNNKYAASSYLSLTPEQWK (7), SYSCQVTHEGSTVEK (7), YAASSYLSLTPEQWK (7)
HPP 53	4	6	SNNKYAASSYLSLTPEQWK (8)
HPP 54	9	9	IHERTHIGQK (8)
HPP 54	9	11	IHERTHIGQK (14)
HPP 54	13	9	IHERTHIGQK (8)
HPP 54	14	7	IHERTHIGQK (11)
HPP 55	3	17	HLELMISSFLIR (10)
HPP 55	3	25	HLELMISSFLIR (6)
HPP 55	4	13	HLELMISSFLIR (19)
HPP 55	4	23	HLELMISSFLIR (6)
HPP 55	7	22	HLELMISSFLIR (4)
HPP 56	15	12	VLKESEPPK (13)
HPP 57	6	8	LYACEVTHQGLSSPVTK (7)
HPP 57	8	14	DSTYSLSSTLTLSK (9), LYACEVTHQGLSSPVTK (9), SGTASVVCLLNNFYPR (9), TVAAPSVFIFPPSDEQLK (9), VDNALQSGNSQESVTEQDSK (9)
HPP 57	8	22	LYACEVTHQGLSSPVTK (2)
HPP 58	3	11	VQEGYTCDCFDGYHLDTAK (9)
HPP 58	3	12	CLCLPGYVPSDKPNYCTPLNTALNLEK (7)
HPP 58	4	9	MTCVDVNECDELNNR (14), VQEGYTCDCFDGYHLDTAK (13-14)
HPP 58	4	10	VQEGYTCDCFDGYHLDTAK (8)
HPP 58	4	11	VQEGYTCDCFDGYHLDTAK (8)
HPP 58	4	12	VQEGYTCDCFDGYHLDTAK (6-7)
HPP 59	12	16	RPSGNLVSVLSGAEGSFVSSLVK (8)
HPP 59	12	17	RPSGNLVSVLSGAEGSFVSSLVK (8)
HPP 59	13	16	RPSGNLVSVLSGAEGSFVSSLVK (8)
HPP 59	13	17	RPSGNLVSVLSGAEGSFVSSLVK (9)
HPP 60	3	9	EEIVYLPCIYR (16-17), NTGTEAPDYLATVDVDPK (16)
HPP 60	3	10	NTGTEAPDYLATVDVDPK (12)
HPP 60	5	9	SPQYCQVIHR (14-15)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 60	14	18	GGFVLLDGETFEVK (10), GGPVQVLEDEELK (10)
HPP 60	15	9	SPQYCQVIHR (15)
HPP 61	10	23	AWILERAFPQCLR (5)
HPP 61	10	25	AWILERAFPQCLR (4)
HPP 61	14	27	AWILERAFPQCLR (6, 8, 12, 13)
HPP 61	14	28	AWILERAFPQCLR (6-7)
HPP 61	15	24	AWILERAFPQCLR (12)
HPP 62	6	13	AQSQLVAGIK (13), VTGDHVDLTTCPLAAGAQQEK (11-13)
HPP 62	6	15	VTGDHVDLTTCPLAAGAQQEK (9)
HPP 62	7	13	VTGDHVDLTTCPLAAGAQQEK (13)
HPP 63	1	5	ASEGGFTATGQR (23)
HPP 63	1	7	ASEGGFTATGQR (10)
HPP 63	18	12	FSCFQEEAPQPHYQLR (10)
HPP 63	18	13	ELLALIQLER (11), EVGPPLPQEAVPLQK (9), LTFINDLCGPR (10-12)
HPP 63	18	19	FSCFQEEAPQPHYQLR (4)
HPP 64	9	20	AIQDGTIVLMGTYDDGATK (8), ICLEDNVLMSGVK (8)
HPP 64	10	19	ICLEDNVLMSGVK (7), LIADLGSTSITNLGFR (7)
HPP 64	10	21	ICLEDNVLMSGVK (7-8), LIADLGSTSITNLGFR (8)
HPP 64	10	22	AIQDGTIVLMGTYDDGATK (6-7), DNWVFCGGK (7), ICLEDNVLMSGVK (6-7), LIADLGSTSITNLGFR (5-6), MASGAANVVGPK (5-6), SPFEQHIK (5-7), YFDMWGGDVAPFIEFLK (5-7)
HPP 64	11	18	ICLEDNVLMSGVK (7)
HPP 64	11	21	AIQDGTIVLMGTYDDGATK (8-9), DNWVFCGGK (8-9), ICLEDNVLMSGVK (7-8), LIADLGSTSITNLGFR (7-8), MASGAANVVGPK (8-9), SPFEQHIK (7), YFDMWGGDVAPFIEFLK (7-8)
HPP 64	11	22	LIADLGSTSITNLGFR (7), YFDMWGGDVAPFIEFLK (7)
HPP 64	12	21	AIQDGTIVLMGTYDDGATK (7-8), ICLEDNVLMSGVK (7-8), LIADLGSTSITNLGFR (8), MASGAANVVGPK (7-8), SPFEQHIK (7), YFDMWGGDVAPFIEFLK (8)
HPP 64	12	22	ICLEDNVLMSGVK (6), MASGAANVVGPK (5)
HPP 64	13	22	AIQDGTIVLMGTYDDGATK (6), DNWVFCGGK (6-7), GINVALANGK (6), ICLEDNVLMSGVK (6), LIADLGSTSITNLGFR (6-7), MASGAANVVGPK (6), SPFEQHIK (6), YFDMWGGDVAPFIEFLK (6-7)
HPP 64	13	23	AIQDGTIVLMGTYDDGATK (7), ICLEDNVLMSGVK (7), YFDMWGGDVAPFIEFLK (7)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 65	13	8	AAGRLSIHSLEAQSLR (8)
HPP 65	14	6	AAGRLSIHSLEAQSLR (12), LSIHSLEAQSLR (10)
HPP 65	15	6	AAGRLSIHSLEAQSLR (9-11), LSIHSLEAQSLR (9-10)
HPP 65	16	6	AAGRLSIHSLEAQSLR (7, 9, 10, 11), LSIHSLEAQSLR (7, 9, 10)
HPP 65	16	7	LSIHSLEAQSLR (10, 12)
HPP 65	16	8	AAGRLSIHSLEAQSLR (6), LSIHSLEAQSLR (6)
HPP 65	16	9	LSIHSLEAQSLR (7)
HPP 65	16	13	AAGRLSIHSLEAQSLR (8)
HPP 66	2	13	VTVLGQPK (12)
HPP 66	3	14	ANPTVTLFPPSSEELQANK (7), SYSCQVTHEGSTVEK (7-8), VTVLGQPK (7-8), YAASSYLSLTPEQWK (7-8)
HPP 66	3	15	VTVLGQPK (8-9), YAASSYLSLTPEQWK (8-9)
HPP 66	4	17	QSNNKYAASSYLSLTPEQWK (7), SYSCQVTHEGSTVEK (7), VTVLGQPK (7)
HPP 66	6	12	VTVLGQPK (9), YAASSYLSLTPEQWK (9)
HPP 66	6	13	ANPTVTLFPPSSEELQANK (10), ATLVCLISDFYPGAVTVAWK (12), SYSCQVTHEGSTVEK (11-12), VTVLGQPK (10-12), YAASSYLSLTPEQWK (10-12)
HPP 66	6	14	ATLVCLISDFYPGAVTVAWK (8), VTVLGQPK (8), YAASSYLSLTPEQWK (8)
HPP 66	7	13	SYSCQVTHEGSTVEK (11-12), VTVLGQPK (11-12), YAASSYLSLTPEQWK (12)
HPP 66	8	15	SYSCQVTHEGSTVEK (14), VTVLGQPK (14), YAASSYLSLTPEQWK (14)
HPP 67	3	13	ANPTVTLFPPSSEELQANK (14), ATLVCLISDFYPGAVTVAWK (14), SYSCQVTHEGSTVEK (14), YAASSYLSLTPEQWK (14)
HPP 67	4	13	ANPTVTLFPPSSEELQANK (11-13), ATLVCLISDFYPGAVTVAWK (11-13), SYSCQVTHEGSTVEK (11-13), YAASSYLSLTPEQWK (11-13)
HPP 67	5	14	ANPTVTLFPPSSEELQANK (7), SYSCQVTHEGSTVEK (7), YAASSYLSLTPEQWK (7)
HPP 67	8	14	ANPTVTLFPPSSEELQANK (6), ATLVCLISDFYPGAVTVAWK (6), SYSCQVTHEGSTVEK (6)
HPP 67	9	5	SYSCQVTHEGSTVEK (11)
HPP 67	9	16	ATLVCLISDFYPGAVTVAWK (8)
HPP 67	9	23	SYSCQVTHEGSTVEK (3)
HPP 68	1	15	LTVLGQPK (9)
HPP 68	1	16	LTVLGQPK (8)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 68	2	12	LTVLGQPK (12, 14, 16)
HPP 68	2	13	LTVLGQPK (14, 17)
HPP 68	2	22	LTVLGQPK (2-3)
HPP 68	3	14	LTVLGQPK (6-7, 9)
HPP 68	3	15	LTVLGQPK (8)
HPP 68	3	17	LTVLGQPK (7)
HPP 68	3	23	LTVLGQPK (2)
HPP 68	4	24	LTVLGQPK (1)
HPP 68	5	14	LTVLGQPK (7)
HPP 68	5	19	LTVLGQPK (5)
HPP 68	5	28	LTVLGQPK (2)
HPP 68	6	13	LTVLGQPK (9-13)
HPP 68	6	14	LTVLGQPK (8-9)
HPP 68	6	18	LTVLGQPK (5)
HPP 68	7	12	LTVLGQPK (12)
HPP 68	8	14	LTVLGQPK (7)
HPP 68	8	15	LTVLGQPK (6, 8, 14, 15)
HPP 68	9	12	LTVLGQPK (11)
HPP 68	9	14	LTVLGQPK (8)
HPP 68	10	14	LTVLGQPK (8, 10)
HPP 68	13	15	LTVLGQPK (9)
HPP 69	14	24	ILTCMQGMEEIR (1)
HPP 69	15	15	ILTCMQGMEEIR (12)
HPP 70	6	8	VVEPPEKDDQLVVLFPVQKPK (8)
HPP 70	6	10	AWMETEDTLGR (8)
HPP 70	7	9	VVEPPEKDDQLVVLFPVQKPK (12)
HPP 70	8	10	AWMETEDTLGR (8), VVEPPEKDDQLVVLFPVQKPK (8)
HPP 70	8	11	AWMETEDTLGR (8-9), HWPSEQDPEKAWGAR (8), LLTTEEKPR (8), LWVMPNHQVLLGPEEDQDHIYHPQ (8), VVEPPEKDDQLVVLFPVQKPK (8)
HPP 70	9	8	LLTTEEKPR (11-13), VVEPPEKDDQLVVLFPVQKPK (12)
HPP 70	9	9	AWMETEDTLGR (11, 13, 14, 15), GPILPGTK (13), HWPSEQDPEK (14), HWPSEQDPEKAWGAR (12), LLTTEEKPR (10, 13, 15, 17), VVEPPEKDDQLVVLFPVQKPK (11-15)

Table 3

Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 70	9	10	AWMETEDTLGR (9-11, 13, 14), DDQLVVLFPVQKPK (9-10), LWVMPNHQVLLGPEEDQDHIYHPQ (10), VVEPPEKDDQLVVLFPVQKPK (11)
HPP 70	9	11	AWMETEDTLGR (9-11, 13), GPILPGTK (11-12), HWPSEQDPEKAWGAR (11), LLTTEEKPR (10-12), LLTTEEKPRGQGR (11), LWVMPNHQVLLGPEEDQDHIYHPQ (11-12), VLSPEPDHDSLYHPPPEEDQGEERPR (11), VVEPPEKDDQLVVLFPVQKPK (10-11)
HPP 70	10	9	AWMETEDTLGR (15-18), LLTTEEKPR (14-16), VVEPPEKDDQLVVLFPVQKPK (17)
HPP 70	10	10	AWMETEDTLGR (8, 10, 11), HWPSEQDPEK (10), LLTTEEKPR (10), LWVMPNHQVLLGPEEDQDHIYHPQ (10-11), VVEPPEKDDQLVVLFPVQKPK (9-11)
HPP 70	10	11	AWMETEDTLGR (8), VVEPPEKDDQLVVLFPVQKPK (11)
HPP 70	11	9	LLTTEEKPR (14), VVEPPEKDDQLVVLFPVQKPK (16-17)
HPP 70	11	10	AWMETEDTLGR (11), LWVMPNHQVLLGPEEDQDHIYHPQ (11), VVEPPEKDDQLVVLFPVQKPK (9, 11)
HPP 71	13	20	KGDTFSCMVGHEALPLAFTQETIDR (6), QEPSQGTTTFAVTSILR (6)
HPP 72	10	21	SRCQLEVK (9)
HPP 73	15	21	MHKAGLLGLCAR (4)
HPP 73	16	18	MHKAGLLGLCAR (16)
HPP 73	17	26	MHKAGLLGLCAR (2)
HPP 74	13	18	SCYLKSGNQK (10)
HPP 75	11	7	SQNYFTNR (12)
HPP 75	12	7	GFEDGDDAISK (8)
HPP 76	8	19	EVMPSIQSLDALVK (5)
HPP 76	8	20	EVMPSIQSLDALVK (5)
HPP 76	8	22	EVMPSIQSLDALVK (3-4), GLMYSVNPNK (4)
HPP 76	8	24	EVMPSIQSLDALVK (3)
HPP 76	8	25	EVMPSIQSLDALVK (3)
HPP 77	1	12	ETSNFGFSLLR (15)
HPP 78	2	21	EFLEDTCVQYVQK (7), TQSGLQSYLLQFHGLVR (7)
HPP 78	2	22	CFLGCELPPEGSR (6), EFLEDTCVQYVQK (6), TQSGLQSYLLQFHGLVR (4, 6)
HPP 78	2	23	EFLEDTCVQYVQK (6), TQSGLQSYLLQFHGLVR (5)

Table 3			
Protein	CEX	RP1	Tryptic Sequence (RP2 fractions)
HPP 79	4	13	DASGVTFTWTPSSGK (11)
HPP 79	9	22	TFTCTAAYPESK (4)
HPP 79	12	20	QEPSQGTTTFAVTSILR (7)

HPP nucleic acids

One aspect of the invention pertains to purified or isolated nucleic acid molecules that encode HPPs or biologically active portions thereof as further described herein, as well as nucleic acid fragments thereof. Said nucleic acids may be used, for example, in detection methods as further described herein.

An object of the invention is a purified, isolated, or recombinant nucleic acid coding for an HPP, complementary sequences thereto, and fragments thereof. The invention also pertains to a purified or isolated nucleic acid comprising a polynucleotide having at least 95% nucleotide identity with a polynucleotide coding for an HPP, advantageously 99 % nucleotide identity, preferably 99.5% nucleotide identity and most preferably 99.8% nucleotide identity with a polynucleotide coding for an HPP, or a sequence complementary thereto or a biologically active fragment thereof. Another object of the invention relates to purified, isolated or recombinant nucleic acids comprising a polynucleotide that hybridizes, under the stringent hybridization conditions defined herein, with a polynucleotide coding for an HPP, or a sequence complementary thereto or a variant thereof or a biologically active fragment thereof.

In another preferred aspect, the invention pertains to purified or isolated nucleic acid molecules that encode a portion or variant of an HPP, wherein the portion or variant displays an HPP biological activity. Preferably said portion or variant is a portion or variant of a naturally occurring HPP or precursor thereof.

Another object of the invention is a purified, isolated, or recombinant nucleic acid encoding an HPP comprising, consisting essentially of, or consisting of the amino acid sequence selected from the group of sequences from Table 3, or fragments thereof, wherein the isolated nucleic acid molecule encodes one or more motifs, such as a target binding site.

A nucleic acid fragment encoding a "biologically active portion of an HPP" can be prepared by isolating a portion of a nucleotide sequence coding for an HPP, which encodes a polypeptide having an HPP biological activity, expressing the encoded portion of the HPP (e.g., by recombinant expression in vitro or in vivo) and assessing the activity of the encoded portion of the HPP.

The invention further encompasses nucleic acid molecules that differ from the HPP nucleotide sequences of the invention due to degeneracy of the genetic code and encode the same HPPs of the invention.

In addition to the HPP nucleotide sequences described above, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of the HPPs may exist within a population (e.g., the human population). Such genetic polymorphism may exist among individuals within a population due to natural allelic variation. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of an HPP-encoding gene or nucleic acid sequence.

Nucleic acid molecules corresponding to natural allelic variants and homologues of the HPP nucleic acids of the invention can be isolated based on their homology to the HPP nucleic acids disclosed herein using the cDNAs disclosed herein, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

It will be appreciated that the invention comprises polypeptides having an amino acid sequence encoded by any of the polynucleotides of the invention.

Uses of HPP nucleic acids

Polynucleotide sequences (or the complements thereof) encoding HPPs have various applications, including uses as hybridization probes. In addition, HPP-encoding nucleic acids are useful for the preparation of HPPs by recombinant techniques, as described herein. The polynucleotides described herein, including sequence variants thereof, can be used in detection assays. Accordingly, detecting the presence of such polynucleotides in body fluids or tissue samples is a feature of the present invention. Examples of nucleic acid based detection assays in accordance with the present invention include, but are not limited to, hybridization assays (e.g., in situ hybridization or nucleotide arrays) and PCR-based assays. Polynucleotides, including extended length polynucleotides, sequence variants and fragments thereof, as described herein, may be used to generate hybridization probes or PCR primers for use in such assays. Such probes and primers will be capable of detecting polynucleotide sequences, including genomic sequences that are similar, or complementary to, the HPP polynucleotides described herein.

The invention includes primer pairs for carrying out a PCR to amplify a segment of a polynucleotide of the invention. Each primer of a pair is an oligonucleotide having a length of between 15 and 30 nucleotides such that i) one primer of the pair forms a perfectly matched duplex with one strand of a polynucleotide of the invention and the other primer of the pair form a perfectly

match duplex with the complementary strand of the same polynucleotide, and ii) the primers of a pair form such perfectly matched duplexes at sites on the polynucleotide that separated by a distance of between 10 and 2500 nucleotides. Preferably, the annealing temperature of each primer of a pair to its respective complementary sequence is substantially the same.

Hybridization probes derived from polynucleotides of the invention can be used, for example, in performing in situ hybridization on tissue samples, such as fixed or frozen tissue sections prepared on microscopic slides or suspended cells. Briefly, a labeled DNA or RNA probe is allowed to bind its DNA or RNA target sample in the tissue section on a prepared microscopic, under controlled conditions. Generally, dsDNA probes consisting of the DNA of interest cloned into a plasmid or bacteriophage DNA vector are used for this purpose, although ssDNA or ssRNA probes may also be used. Probes are generally oligonucleotides between about 15 and 40 nucleotides in length. Alternatively, the probes can be polynucleotide probes generated by PCR random priming primer extension or in vitro transcription of RNA from plasmids (riboprobes). These latter probes are typically several hundred base pairs in length. The probes can be labeled by any of a number of label groups and the particular detection method will correspond to the type of label utilized on the probe (e.g., autoradiography, X-ray detection, fluorescent or visual microscopic analysis, as appropriate). The reaction can be further amplified in situ using immunocytochemical techniques directed against the label of the detector molecule used, such as an antibody directed to a fluorescein moiety present on a fluorescently labeled probe. Specific labeling and in situ detection methods can be found, for example, in Howard, G. C., Ed., *Methods in Nonradioactive Detection,* Appleton & Lange, Norwalk, Conn., (1993), herein incorporated by reference.

Hybridization probes and PCR primers may also be selected from the genomic sequences corresponding to the full-length proteins identified in accordance with the present invention, including promoter, enhancer elements and introns of the gene encoding the naturally occurring polypeptide. Nucleotide sequences encoding an HPP can also be used to construct hybridization probes for mapping the gene encoding that HPP and for the genetic analysis of individuals. Individuals carrying variations of, or mutations in the gene encoding an HPP of the present invention may be detected at the DNA level by a variety of techniques. Nucleic acids used for diagnosis may be obtained from a patient's cells, including, for example, tissue biopsy and autopsy material. Genomic DNA may be used directly for detection or may be amplified enzymatically by using PCR (Saiki, et al. *Nature* 324:163-166 (1986)) prior to analysis. RNA or cDNA may also be used for the same purpose. As an example, PCR primers complementary to the nucleic acid of the present invention can be used to identify and analyze mutations in the gene of the present invention. Deletions and insertions can be

detected by a change in size of the amplified product in comparison to the normal genotype. Point mutations can be identified by hybridizing amplified DNA to radiolabeled RNA of the invention or alternatively, radiolabeled antisense DNA sequences of the invention. Sequence changes at specific locations may also be revealed by nuclease protection assays, such as RNase and Sl protection or the chemical cleavage method (e.g. Cotton, et al., *Proc. Natl. Acad. Sci. USA* 85:4397-4401 (1985)), or by differences in melting temperatures. "Molecular beacons" (Kostrikis L. G. et al., *Science* 279:1228-1229 (1998)), hairpin-shaped, single-stranded synthetic oligonucleotides containing probe sequences which are complementary to the nucleic acid of the present invention, may also be used to detect point mutations or other sequence changes as well as monitor expression levels of HPPs.

Nucleotides of the invention, including PCR primers and probes, may be synthesized by conventional means on a commercially available automated DNA synthesizer, e.g. an Applied Biosystems (Foster City, CA) model 380B, 392 or 394 DNA/RNA synthesizer. Preferably, phosphoramidite chemistry is employed, e.g. as disclosed in the following references: Beaucage and Iyer, Tetrahedron, 48: 2223-2311 (1992); Molko et al, U.S. patent 4,980,460; Koster et al, U.S. patent 4,725,677; Caruthers et al, U.S. patents 4,415,732; 4,458,066; and 4,973,679.

Primers and probes of the invention can also be prepared by, for example, cloning and restriction of appropriate sequences and direct chemical synthesis by a method such as the phosphodiester method of Narang SA et al (Methods Enzymol 1979; 68:90-98), the phosphodiester method of Brown EL et al (Methods Enzymol 1979; 68:109-151), the diethylphosphoramidite method of Beaucage et al (Tetrahedron Lett 1981, 22: 1859-1862) and the solid support method described in EP 0 707 592.

Detection probes are generally nucleic acid sequences or uncharged nucleic acid analogs such as peptide nucleic acids which are disclosed in WO 92/20702, morpholino analogs which are described in U.S. Patents 5,185,444; 5,034,506 and 5,142,047. If desired, the probe may be rendered "non-extendable" in that additional dNTPs cannot be added to the probe. In and of themselves analogs usually are non-extendable and nucleic acid probes can be rendered non-extendable by modifying the 3' end of the probe such that the hydroxyl group is no longer capable of participating in elongation. For example, the 3' end of the probe can be functionalized with the capture or detection label to thereby consume or otherwise block the hydroxyl group.

Any of the polynucleotides of the present invention can be labeled, if desired, by incorporating any label group known in the art to be detectable by spectroscopic, photochemical, biochemical, immunochemical, or chemical means. Additional examples include non-radioactive labeling of nucleic acid fragments as described in Urdea et al. (Nucleic Acids Research. 11:4937-4957, 1988) or

Sanchez-Pescador et al. (J. Clin. Microbiol. 26(10):1934-1938, 1988). In addition, the probes according to the present invention may have structural characteristics such that they allow the signal amplification, such structural characteristics being, for example, branched DNA probes as those described by Urdea et al (Nucleic Acids Symp. Ser. 24:197-200, 1991) or in the European patent No. EP 0225807 (Chiron).

A label can also be used to capture the primer, so as to facilitate the immobilization of either the primer or a primer extension product, such as amplified DNA, on a solid support. A capture label is attached to the primers or probes and can be a specific binding member which forms a binding pair with the solid's phase reagent's specific binding member (e.g. biotin and streptavidin). Therefore depending upon the type of label carried by a polynucleotide or a probe, it may be employed to capture or to detect the target DNA. Further, it will be understood that the polynucleotides, primers or probes provided herein, may, themselves, serve as the capture label. For example, in the case where a solid phase reagent's binding member is a nucleic acid sequence, it may be selected such that it binds a complementary portion of a primer or probe to thereby immobilize the primer or probe to the solid phase. In cases where a polynucleotide probe itself serves as the binding member, those skilled in the art will recognize that the probe will contain a sequence or "tail" that is not complementary to the target. In the case where a polynucleotide primer itself serves as the capture label, at least a portion of the primer will be free to hybridize with a nucleic acid on a solid phase. DNA labeling techniques are well known to the skilled technician.

The probes of the present invention are useful for a number of purposes. They can be notably used in Southern hybridization to genomic DNA. The probes can also be used to detect PCR amplification products. They may also be used to detect mismatches in HPP-encoding genes or mRNA using other techniques.

Any of the nucleic acids, polynucleotides, primers and probes of the present invention can be conveniently immobilized on a solid support. Solid supports are known to those skilled in the art and include the walls of wells of a reaction tray, test tubes, polystyrene beads, magnetic beads, nitrocellulose strips, membranes, microparticles such as latex particles, sheep (or other animal) red blood cells, duracytes and others. The solid support is not critical and can be selected by one skilled in the art. Thus, latex particles, microparticles, magnetic or non-magnetic beads, membranes, plastic tubes, walls of microtiter wells, glass or silicon chips, sheep (or other suitable animal's) red blood cells and duracytes are all suitable examples. Suitable methods for immobilizing nucleic acids on solid phases include ionic, hydrophobic, covalent interactions and the like. A solid support, as used herein, refers to any material which is insoluble, or can be made insoluble by a subsequent reaction.

The solid support can be chosen for its intrinsic ability to attract and immobilize the capture reagent. Alternatively, the solid phase can retain an additional receptor which has the ability to attract and immobilize the capture reagent. The additional receptor can include a charged substance that is oppositely charged with respect to the capture reagent itself or to a charged substance conjugated to the capture reagent. As yet another alternative, the receptor molecule can be any specific binding member attached to the solid support and which has the ability to immobilize the capture reagent through a specific binding reaction. The receptor molecule enables the indirect binding of the capture reagent to a solid support material before the performance of the assay or during the performance of the assay. The solid phase thus can be a plastic, derivatized plastic, magnetic or non-magnetic metal, glass or silicon surface of a test tube, microtiter well, sheet, bead, microparticle, chip, sheep (or other suitable animal's) red blood cells, duracytes and other configurations known to those of ordinary skill in the art. The nucleic acids, polynucleotides, primers and probes of the invention can be attached to or immobilized on a solid support individually or in groups of at least 2, 5, 8, 10, 12, 15, 20, or 25 distinct polynucleotides of the invention to a single solid support. In addition, polynucleotides other than those of the invention may be attached to the same solid support as one or more polynucleotides of the invention.

Any polynucleotide provided herein may be attached in overlapping areas or at random locations on a solid support. Alternatively the polynucleotides of the invention may be attached in an ordered array wherein each polynucleotide is attached to a distinct region of the solid support which does not overlap with the attachment site of any other polynucleotide. Preferably, such an ordered array of polynucleotides is designed to be "addressable" where the distinct locations are recorded and can be accessed as part of an assay procedure. Addressable polynucleotide arrays typically comprise a plurality of different oligonucleotide probes that are coupled to a surface of a substrate in different known locations. The knowledge of the precise location of each polynucleotides location makes these "addressable" arrays particularly useful in hybridization assays. Any addressable array technology known in the art can be employed with the polynucleotides of the invention. One particular embodiment of these polynucleotide arrays is known as the Genechips, and has been generally described in US Patent 5,143,854; PCT publications WO 90/15070 and 92/10092. Preferably, more than one HPP polynucleotide probe is included in such an array.

Methods for obtaining variant nucleic acids and polypeptides

In addition to naturally-occurring allelic variants of the HPP sequences that may exist in the population, the skilled artisan will appreciate that changes can be introduced by mutation into the

nucleotide sequences coding for HPPs, thereby leading to changes in the amino acid sequence of the encoded HPPs, with or without altering the functional ability of the HPPs.

Several types of variants are contemplated including 1) one in which one or more of the amino acid residues are substituted with a conserved or non-conserved amino acid residue and such substituted amino acid residue may or may not be one encoded by the genetic code, or 2) one in which one or more of the amino acid residues includes a substituent group, or 3) one in which the mutated HPP is fused with another compound, such as a compound to increase the half-life of the polypeptide (for example, polyethylene glycol), or 4) one in which the additional amino acids are fused to the HPP, such as a leader, a signal or anchor sequence, a sequence which is employed for purification of the HPP, or sequence from a precursor protein. Such variants are deemed to be within the scope of those skilled in the art.

The invention provides HPP chimeric or fusion proteins. As used herein, an HPP "chimeric protein" or "fusion protein" comprises an HPP of the invention or fragment thereof, operatively linked or fused in frame to a non-HPP polypeptide sequence. In a preferred embodiment, an HPP fusion protein comprises at least one biologically active portion of an HPP. In another preferred embodiment, an HPP fusion protein comprises at least two biologically active portions of an HPP. For example, in one embodiment, the fusion protein is a GST-HPP fusion protein in which HPP domain sequences are fused to the C-terminus of the GST sequences. Such fusion proteins can facilitate the purification of recombinant HPPs. In another embodiment, the fusion protein is an HPP containing a heterologous signal sequence at its N-terminus, for example, to allow for a desired cellular localization in a certain host cell. In yet another embodiment, the fusion is an HPP biologically active fragment and an immunoglobulin molecule. Such fusion proteins are useful, for example, to increase the valency of HPP binding sites. For example, a bivalent HPP binding site may be formed by fusing biologically active HPP fragments to an IgG Fc protein.

In a preferred embodiment, HPP fusion proteins of the invention are used as immunogens to produce anti-HPP antibodies in a subject, to purify HPP, or HPP ligands and adsorbants.

Furthermore, isolated fragments of HPPs can also be obtained by screening peptides recombinantly produced from the corresponding fragment of the nucleic acid encoding such peptides. In addition, fragments can be chemically synthesized using techniques known in the art such as conventional Merrifield solid phase f-Moc or t-Boc chemistry. For example, an HPP of the present invention may be arbitrarily divided into fragments of desired length with no overlap of the fragments, or preferably divided into overlapping fragments of a desired length. The fragments can be produced (recombinantly or by chemical synthesis) and tested to identify those peptidyl fragments with an HPP

biological activity, for example, by microinjection assays or in vitro protein binding assays. In an illustrative embodiment, peptidyl portions of an HPP, such as an HPP target binding region, can be tested for HPP activity (e.g., immunogenicity) by expression as thioredoxin fusion proteins, each of which contains a discrete fragment of the HPP (see, for example, U.S. Patents 5, 270,181 and 5,292,646; and WO94/02502).

Chemical Manufacture of HPP Compositions

Peptides of the invention are synthesized by standard techniques (e.g. Stewart and Young, Solid Phase Peptide Synthesis, 2nd Ed., Pierce Chemical Company, Rockford, IL, 1984). Preferably, a commercial peptide synthesizer is used, e.g. Applied Biosystems, Inc. (Foster City, CA) model 430A, and polypeptides of the invention may be assembled from multiple, separately synthesized and purified, peptide in a convergent synthesis approach, e.g. Kent et al, U.S. patent 6,184,344 and Dawson and Kent, Annu. Rev. Biochem., 69: 923-960 (2000). Peptides of the invention may be assembled by solid phase synthesis on a cross-linked polystyrene support starting from the carboxyl terminal residue and adding amino acids in a stepwise fashion until the entire peptide has been formed. The following references are guides to the chemistry employed during synthesis: Schnolzer et al, Int. J. Peptide Protein Res., 40: 180-193 (1992); Merrifield, J. Amer. Chem. Soc., Vol. 85, pg. 2149 (1963); Kent et al., pg 185, in Peptides 1984, Ragnarsson, Ed. (Almquist and Weksell, Stockholm, 1984); Kent et al., pg. 217 in Peptide Chemistry 84, Izumiya, Ed. (Protein Research Foundation, B.H. Osaka, 1985); Merrifield, Science, Vol. 232, pgs. 341-347 (1986); Kent, Ann. Rev. Biochem, Vol. 57, pgs. 957-989 (1988), and references cited in these latter two references.

Preferably, chemical synthesis of polypeptides of the invention is carried out by the assembly of peptide fragments by native chemical ligation, as described by Dawson et al, Science, 266: 776-779 (1994) and Kent el al, U.S. patent 6,184,344. Briefly, in the approach a first peptide fragment is provided with an N-terminal cysteine having an unoxidized sulfhydryl side chain, and a second peptide fragment is provided with a C-terminal thioester. The unoxidized sulfhydryl side chain of the N-terminal cysteine is then condensed with the C-terminal thioester to produce an intermediate peptide fragment which links the first and second peptide fragments with a β-aminothioester bond. The β-aminothioester bond of the intermediate peptide fragment then undergoes an intramolecular rearrangement to produce the peptide fragment product which links the first and second peptide fragments with an amide bond. Preferably, the N-terminal cysteine of the internal fragments is protected from undesired cyclization and/or concatenation reactions by a cyclic thiazolidine protecting group as described below. Preferably, such cyclic thiazolidine protecting group is a

thioprolinyl group.

Peptide fragments having a C-terminal thioester may be produced as described in the following references, which are incorporated by reference: Kent et al, U.S. patent 6,184,344; Tam et al, Proc. Natl. Acad. Sci., 92: 12485-12489 (1995); Blake, Int. J. Peptide Protein Res., 17: 273 (1981); Canne et al, Tetrahedron Letters, 36: 1217-1220 (1995); Hackeng et al, Proc. Natl. Acad. Sci., 94: 7845-7850 (1997); or Hackeng et al, Proc. Natl. Acad. Sci., 96: 10068-10073 (1999). Preferably, the method described by Hackeng et al (1999) is employed. Briefly, peptide fragments are synthesized on a solid phase support (described below) typically on a 0.25 mmol scale by using the in situ neutralization/HBTU activation procedure for Boc chemistry disclosed by Schnolzer et al, Int. J. Peptide Protein Res., 40: 180-193 (1992), which reference is incorporated herein by reference. (HBTU is 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate and Boc is tert-butoxycarbonyl). Each synthetic cycle consists of N^{α}-Boc removal by a 1- to 2- minute treatment with neat TFA, a 1-minute DMF flow wash, a 10- to 20-minute coupling time with 1.0 mmol of preactivated Boc-amino acid in the presence of DIEA, and a second DMF flow wash. (TFA is trifluoroacetic acid, DMF is N,N-dimethylformamide, and DIEA is N,N-diisopropylethylamine). N^{α}-Boc-amino acids (1.1 mmol) are preactivated for 3 minutes with 1.0 mmol of HBTU (0.5 M in DMF) in the presence of excess DIEA (3 mmol). After each coupling step, yields are determined by measuring residual free amine with a conventional quantitative ninhydrin assay, e.g. as disclosed in Sarin et al, Anal. Biochem., 117: 147-157 (1981). After coupling of Gln residues, a DCM flow wash is used before and after deprotection by using TFA, to prevent possible high-temperature (TFA/DMF)-catalyzed pyrrolidone formation. After chain assembly is completed, the peptide fragments are deprotected and cleaved from the resin by treatment with anhydrous HF for 1 hour at 0°C with 4% *p*-cresol as a scavenger. The imidazole side-chain 2,4-dinitrophenyl (dnp) protecting groups remain on the His residues because the dnp-removal procedure is incompatible with C-terminal thioester groups. However, dnp is gradually removed by thiols during the ligation reaction. After cleavage, peptide fragments are precipitated with ice-cold diethylether, dissolved in aqueous acetonitrile, and lyophilized.

Thioester peptide fragments described above are preferably synthesized on a trityl-associated mercaptopropionic acid-leucine (TAMPAL) resin, made as disclosed by Hackeng et al (1999), or comparable protocol. Briefly, N^{α}-Boc-Leu (4 mmol) is activated with 3.6 mmol of HBTU in the presence of 6 mmol of DIEA and coupled for 16 minutes to 2 mmol of p-methylbenzhydrylamine (MBHA) resin, or the equivalent. Next, 3 mmol of S-trityl mercaptopropionic acid is activated with 2.7 mmol of HBTU in the presence of 6 mmol of DIEA and coupled for 16 minutes to Leu-MBHA

resin. The resulting TAMPAL resin can be used as a starting resin for polypeptide-chain assembly after removal of the trityl protecting group with two 1-minute treatments with 3.5% triisopropylsilane and 2.5% H_2O in TFA. The thioester bond can be formed with any desired amino acid by using standard in situ-neutralization peptide coupling protocols for 1 hour, as disclosed in Schnolzer et al (cited above). Treatment of the final peptide fragment with anhydrous HF yields the C-terminal activated mercaptopropionic acid-leucine (MPAL) thioester peptide fragments.

Preferably, thiazolidine-protected thioester peptide fragment intermediates are used in native chemical ligation under conditions as described by Hackeng et al (1999), or like conditions. Briefly, 0.1 M phosphate buffer (pH 8.5) containing 6 M guanidine, 4% (vol/vol) benzylmercaptan, and 4% (vol/vol) thiophenol is added to dry peptides to be ligated, to give a final peptide concentration of 1-3 mM at about pH 7, lowered because of the addition of thiols and TFA from the lyophilized peptide. Preferably, the ligation reaction is performed in a heating block at 37°C and is periodically vortexed to equilibrate the thiol additives. The reaction may be monitored for degree of completion by MALDI-MS or HPLC and electrospray ionization MS.

After a native chemical ligation reaction is completed or stopped, the N-terminal thiazolidine ring of the product is opened by treatment with a cysteine deprotecting agent, such as O-methylhydroxylamine (0.5 M) at pH 3.5-4.5 for 2 hours at 37° C, after which a 10-fold excess of Tris-(2-carboxyethyl)-phosphine is added to the reaction mixture to completely reduce any oxidizing reaction constituents prior to purification of the product by conventional preparative HPLC. Preferably, fractions containing the ligation product are identified by electrospray MS, are pooled, and lyophilized.

After the synthesis is completed and the final product purified, the final polypeptide product may be refolded by conventional techniques, e.g. Creighton, Meth. Enzymol., 107: 305-329 (1984); White, Meth. Enzymol., 11: 481-484 (1967); Wetlaufer, Meth. Enzymol., 107: 301-304 (1984); and the like. Preferably, a final product is refolded by air oxidation by the following, or like: The reduced lyophilized product is dissolved (at about 0.1 mg/mL) in 1 M guanidine hydrochloride (or like chaotropic agent) with 100 mM Tris, 10 mM methionine, at pH 8.6. After gentle overnight stirring, the re-folded product is isolated by reverse phase HPLC with conventional protocols.

Recombinant Expression Vectors and Host Cells

The polynucleotide sequences described herein can be used in recombinant DNA molecules that direct the expression of the corresponding polypeptides in appropriate host cells. Because of the degeneracy in the genetic code, other DNA sequences may encode the equivalent amino acid

sequence, and may be used to clone and express the HPPs. Codons preferred by a particular host cell may be selected and substituted into the naturally occurring nucleotide sequences, to increase the rate and/or efficiency of expression. The nucleic acid (e.g., cDNA or genomic DNA) encoding the desired HPP may be inserted into a replicable vector for cloning (amplification of the DNA), or for expression. The polypeptide can be expressed recombinantly in any of a number of expression systems according to methods known in the art (Ausubel, et al., editors, Current Protocols in Molecular Biology, John Wiley & Sons, New York, 1990). Appropriate host cells include yeast, bacteria, archebacteria, fungi, and insect and animal cells, including mammalian cells, for example primary cells, including stem cells, including, but not limited to bone marrow stem cells. More specifically, these include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid or cosmid DNA expression vectors, and yeast transformed with yeast expression vectors. Also included, are insect cells infected with a recombinant insect virus (such as baculovirus), and mammalian expression systems. The nucleic acid sequence to be expressed may be inserted into the vector by a variety of procedures. In general, DNA is inserted into an appropriate restriction endonuclease site using techniques known in the art. Vector components generally include, but are not limited to, one or more of a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination sequence. Construction of suitable vectors containing one or more of these components employs standard ligation techniques which are known to the skilled artisan.

The HPPs of the present invention are produced by culturing a host cell transformed with an expression vector containing a nucleic acid encoding an HPP, under the appropriate conditions to induce or cause expression of the protein. The conditions appropriate for HPP expression will vary with the choice of the expression vector and the host cell, as ascertained by one skilled in the art. For example, the use of constitutive promoters in the expression vector may require routine optimization of host cell growth and proliferation, while the use of an inducible promoter requires the appropriate growth conditions for induction. In addition, in some embodiments, the timing of the harvest is important. For example, the baculoviral systems used in insect cell expression are lytic viruses, and thus harvest time selection can be crucial for product yield.

A host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the protein include, but are not limited to, glycosyl, acetyl, phosphate, amide, lipid, carboxyl, acyl, or carbohydrate groups. Post-translational processing, which cleaves a "prepro" form of the protein, may also be important for correct insertion, folding and/or function. By way of example, host cells such as

CHO, HeLa, BHK, MDCK, 293, W138, etc. have specific cellular machinery and characteristic mechanisms for such post-translational activities and may be chosen to ensure the correct modification and processing of the introduced, foreign protein. Of particular interest are *Drosophila melanogaster* cells, *Saccharomyces cerevisiae* and other yeasts, *E. coli, Bacillus subtilis,* SF9 cells, C129 cells, 293 cells, Neurospora, BHK, CHO, COS, and HeLa cells, fibroblasts, Schwanoma cell lines, immortalized mammalian myeloid and lymphoid cell lines, Jurkat cells, human cells and other primary cells.

The nucleic acid encoding an HPP must be "operably linked" by placing it into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, "operably linked" DNA sequences are contiguous, and, in the case of a secretory leader or other polypeptide sequence, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice. Promoter sequences encode either constitutive or inducible promoters. The promoters may be either naturally occurring promoters or hybrid promoters. Hybrid promoters, which combine elements of more than one promoter, are also known in the art, and are useful in the present invention. The expression vector may comprise additional elements, for example, the expression vector may have two replication systems, thus allowing it to be maintained in two organisms, for example in mammalian or insect cells for expression and in a procaryotic host for cloning and amplification. Both expression and cloning vectors contain a nucleic acid sequence that enables the vector to replicate in one or more selected host cells. Such sequences are well known for a variety of bacteria, yeast, and viruses. The origin of replication from the plasmid pBR322 is suitable for most Gram-negative bacteria, the 2: plasmid origin is suitable for yeast, and various viral origins (SV40, polyoma, adenovirus, VSV or BPV) are useful for cloning vectors in mammalian cells. Further, for integrating expression vectors, the expression vector contains at least one sequence homologous to the host cell genome, and preferably, two homologous sequences which flank the expression construct. The integrating vector may be directed to a specific locus in the host cell by selecting the appropriate homologous sequence for inclusion in the vector. Constructs for integrating vectors are well known in the art. In an additional embodiment, a heterologous expression control element may be operably linked with the endogenous

gene in the host cell by homologous recombination (described in US Patents 6410266 and 6361972). This technique allows one to regulate expression to a desired level with a chosen control element while ensuring proper processing and modification of HPP endogenously expressed by the host cell. Useful heterologous expression control elements include but are not limited to CMV immediate early promoter, the HSV thymidine kinase promoter, the early and late SV40 promoters, the promoters of retroviral LTRs, such as those of the Rous Sarcoma Virus (RSV), and metallothionein promoters.

Preferably, the expression vector contains a selectable marker gene to allow the selection of transformed host cells. Selection genes are well known in the art and will vary with the host cell used. Expression and cloning vectors will typically contain a selection gene, also termed a selectable marker. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxins, e.g., ampicillin, neomycin, methotrexate, or tetracycline, (b) complement auxotrophic deficiencies, or (c) supply critical nutrients not available for from complex media, e.g., the gene encoding D-alanine racemase for Bacilli.

Host cells transformed with a nucleotide sequence encoding an HPP may be cultured under conditions suitable for the expression and recovery of the encoded protein from cell culture. The protein produced by a recombinant cell may be secreted, membrane-bound, or contained intracellularly depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides encoding the HPP can be designed with signal sequences which direct secretion of the HPP through a prokaryotic or eukaryotic cell membrane. The desired HPP may be produced recombinantly not only directly, but also as a fusion polypeptide with a heterologous polypeptide, which may be a signal sequence or other polypeptide having a specific cleavage site at the N-terminus of the mature protein or polypeptide. In general, the signal sequence may be a component of the vector, or it may be a part of the HPP-encoding DNA that is inserted into the vector. The signal sequence may be a prokaryotic signal sequence selected, for example, from the group of the alkaline phosphatase, penicillinase, lpp, or heat-stable enterotoxin II leaders. For yeast secretion the signal sequence may be, e.g., the yeast invertase leader, alpha factor leader (including *Saccharomyces* and *Kluyveromyces* a-factor leaders, the latter described in U.S. Pat. No. 5,010,182), or acid phosphatase leader, the *C. albicans* glucoamylase leader (EP 362,179 published Apr. 4, 1990), or the signal described in WO 90113646 published Nov. 15, 1990. In mammalian cell expression, mammalian signal sequences may be used to direct secretion of the protein, such as signal sequences from secreted polypeptides of the same or related species, as well as viral secretory leaders. According to the expression system selected, the coding sequence is inserted into an appropriate vector, which in turn may require the presence of certain characteristic "control

elements" or "regulatory sequences." Appropriate constructs are known generally in the art (Ausubel, et al., 1990) and, in many cases, are available from commercial suppliers such as Invitrogen (San Diego, Calif.), Stratagene (La Jolla, Calif.), Gibco BRL (Rockville, Md.) or Clontech (Palo Alto, Calif.).

Expression in Bacterial Systems

Transformation of bacterial cells may be achieved using an inducible promoter such as the hybrid lacZ promoter of the "BLUESCRIPT" Phagemid (Stratagene) or "pSPORT1" (Gibco BRL). In addition, a number of expression vectors may be selected for use in bacterial cells to produce cleavable fusion proteins that can be easily detected and/or purified, including, but not limited to "BLUESCRIPT" (a-galactosidase; Stratagene) or pGEX (glutathione S-transferase; Promega, Madison, Wis.). A suitable bacterial promoter is any nucleic acid sequence capable of binding bacterial RNA polymerase and initiating the downstream (3') transcription of the coding sequence of the HPP gene into mRNA. A bacterial promoter has a transcription initiation region which is usually placed proximal to the 5' end of the coding sequence. This transcription initiation region typically includes an RNA polymerase binding site and a transcription initiation site. Sequences encoding metabolic pathway enzymes provide particularly useful promoter sequences. Examples include promoter sequences derived from sugar metabolizing enzymes, such as galactose, lactose and maltose, and sequences derived from biosynthetic enzymes such as tryptophan. Promoters from bacteriophage may also be used and are known in the art. In addition, synthetic promoters and hybrid promoters are also useful; for example, the tat promoter is a hybrid of the trp and lac promoter sequences. Furthermore, a bacterial promoter can include naturally occurring promoters of non-bacterial origin that have the ability to bind bacterial RNA polymerase and initiate transcription. An efficient ribosome-binding site is also desirable. The expression vector may also include a signal peptide sequence that provides for secretion of the HPP in bacteria. The signal sequence typically encodes a signal peptide comprised of hydrophobic amino acids which direct the secretion of the protein from the cell, as is well known in the art. The protein is either secreted into the growth media (gram-positive bacteria) or into the periplasmic space, located between the inner and outer membrane of the cell (gram-negative bacteria). The bacterial expression vector may also include a selectable marker gene to allow for the selection of bacterial strains that have been transformed. Suitable selection genes include drug resistance genes such as ampicillin, chloramphenicol, erythromycin, kanamycin, neomycin and tetracycline. Selectable markers also include biosynthetic genes, such as those in the histidine, tryptophan and leucine biosynthetic pathways. When large quantities of HPPs are needed,

e.g., for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified may be desirable. Such vectors include, but are not limited to, multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the HPP coding sequence may be ligated into the vector in-frame with sequences for the amino-terminal Met and the subsequent 7 residues of beta-galactosidase so that a hybrid protein is produced; PIN vectors (Van Heeke & Schuster *JBiol Chem 264:5503-5509* 1989)); PET vectors (Novagen, Madison Wis.); and the like. Expression vectors for bacteria include the various components set forth above, and are well known in the art. Examples include vectors for *Bacillus subtilis, E. coli, Streptococcus cremoris,* and *Streptococcus lividans,* among others. Bacterial expression vectors are transformed into bacterial host cells using techniques well known in the art, such as calcium chloride mediated transfection, electroporation, and others.

Expression in Yeast

Yeast expression systems are well known in the art, and include expression vectors for *Saccharomyces cerevisiae, Candida albicans* and *C. maltosa, Hansenula polymorpha, Kluyveromyces fragilis* and *K. lactis, Pichia guillermondii* and *P pastoris, Schizosaccharomyces pombe,* and *Yarrowia lipolytica.* Examples of suitable promoters for use in yeast hosts include the promoters for 3-phosphoglycerate kinase (Hitzeman et al., *J. Biol. Chem.* 255:2073 (1980)) or other glycolytic enzymes (Hess et al., J. *Adv. Enzyme Reg.* 7:149 (1968); Holland, *Biochemistry* 17:4900 (1978)), such as enolase, glyceraldehyde-3- phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose- 6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, alpha factor, the ADH2IGAPDH promoter, glucokinase alcohol oxidase, and PGH. See, for example, Ausubel, et al., 1990; Grant et al., *Methods in Enzymology* 153:516-544, (1987). Other yeast promoters, which are inducible have the additional advantage of transcription controlled by growth conditions, include the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, metallothionein, glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization. Suitable vectors andpromoters for use in yeast expression are further described in EP 73,657. Yeast selectable markers include ADE2. HIS4. LEU2. TRPl. and ALG7, which confers resistance to tunicamycin; the neomycin phosphotransferase gene, which confers resistance to G418; and the CUP1 gene, which allows yeast to grow in the presence of copper ions. Yeast expression vectors can be constructed for intracellular production or secretion of an HPP from the DNA encoding the HPP of interest. For example, a selected signal peptide and the

appropriate constitutive or inducible promoter may be inserted into suitable restriction sites in the selected plasmid for direct intracellular expression of the HPP. For secretion of the HPP, DNA encoding the HPP can be cloned into the selected plasmid, together with DNA encoding the promoter, the yeast alpha-factor secretory signal/leader sequence, and linker sequences (as needed), for expression of the HPP. Yeast cells, can then be transformed with the expression plasmids described above, and cultured in an appropriate fermentation media. The protein produced by such transformed yeast can then be concentrated by precipitation with 10% trichloroacetic acid and analyzed following separation by SDS-PAGE and staining of the gels with Coomassie Blue stain. The recombinant HPP can subsequently be isolated and purified from the fermentation medium by techniques known to those of skill in the art.

Expression in Mammalian Systems

The HPP may be expressed in mammalian cells. Mammalian expression systems are known in the art, and include retroviral vector mediated expression systems. Mammalian host cells may be transformed with any of a number of different viral-based expression systems, such as adenovirus, where the coding region can be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a nonessential El or E3 region of the viral genome results in a viable virus capable of expression of the polypeptide of interest in infected host cells. A preferred expression vector system is a retroviral vector system such as is generally described in PCT/US97/01019 and PCT/US97/101048. Suitable mammalian expression vectors contain a mammalian promoter which is any DNA sequence capable of binding mammalian RNA polymerase and initiating the downstream (3') transcription of a coding sequence for HPP into mRNA. A promoter will have a transcription initiating region, which is usually placed proximal to the 5' end of the coding sequence, and a TATA box, using a located 25-30 base pairs upstream of the transcription initiation site. The TATA box is thought to direct RNA polymerase II to begin RNA synthesis at the correct site. A mammalian promoter will also contain an upstream promoter element (enhancer element), typically located within 100 to 200 base pairs upstream of the TATA box. An upstream promoter element determines the rate at which transcription is initiated and can act in either orientation. Of particular use as mammalian promoters are the promoters from mammalian viral genes, since the viral genes are often highly expressed and have a broad host range. Examples include promoters obtained from the genomes of viruses such as polyoma virus, fowlpox virus (UK 2,211, 504 published Jul. 5,1989), adenovirus (such as Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B virus and Simian Virus 40 (SV40), from heterologous

mammalian promoters, e.g., the actin promoter or an immunoglobulin promoter, and from heat-shock promoters, provided such promoters are compatible with the host cell systems. Transcription of DNA encoding an HPP by higher eukaryotes may be increased by inserting an enhancer sequence into the vector. Enhancers are cis-acting elements of DNA, usually about from 10 to 300 bp, that act on a promoter to increase its transcription. Many enhancer sequences are now known from mammalian genes (globin, elastase, albumin, a-fetoprotein, and insulin). Typically, however, one will use an enhancer from a eukaryotic cell virus. Examples include the SV40 enhancer, the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, and adenovirus enhancers. The enhancer is preferably located at a site 5' from the promoter. In general, the transcription termination and polyadenylation sequences recognized by mammalian cells are regulatory regions located 3' to the translation stop codon and thus, together with the promoter elements, flank the coding sequence. The 3' terminus of the mature mRNA is formed by site-specific post-translational cleavage and polyadenylation. Examples of transcription terminator and polyadenylation signals include those derived from SV40. Long term, high-yield production of recombinant proteins can be effected in a stable expression system. Expression vectors which contain viral origins of replication or endogenous expression elements and a selectable marker gene may be used for this purpose. Appropriate vectors containing selectable markers for use in mammalian cells are readily available commercially and are known to persons skilled in the art. Examples of such selectable markers include, but are not limited to herpes simplex virus thymidine kinase and adenine phosphoribosyltransferase for use in tk- or hprt-cells, respectively. The methods of introducing exogenous nucleic acid into mammalian hosts, as well as other hosts, is well known in the art, and will vary with the host cell used. Techniques include dextran-mediated transfection, calcium phosphate precipitation, polybrene mediated transfection, protoplast fusion, electroporation, viral infection, encapsulation of the polynucleotide(s) in liposomes, and direct microinjection of the DNA into nuclei.

HPPs can be purified from culture supernatants of mammalian cells transiently transfected or stably transformed by an expression vector carrying an HPP-encoding sequence. Preferably, HPP is purified from culture supernatants of COS 7 cells transiently transfected by the pcD expression vector. Transfection of COS 7 cells with pcD proceeds as follows: One day prior to transfection, approximately 10^6 COS 7 monkey cells are seeded onto individual 100 mm plates in Dulbecco's modified Eagle medium (DME) containing 10% fetal calf serum and 2 mM glutamine. To perform the transfection, the medium is aspirated from each plate and replaced with 4 ml of DME containing 50 mM Tris.HCl pH 7.4, 400 mg/ml DEAE-Dextran and 50 μg of plasmid DNA. The plates are

incubated for four hours at 37°C, then the DNA-containing medium is removed, and the plates are washed twice with 5 ml of serum-free DME. DME is added back to the plates which are then incubated for an additional 3 hrs at 37°C. The plates are washed once with DME, after which DME containing 4% fetal calf serum, 2 mM glutamine, penicillin (100 U/L) and streptomycin (100 μg/L) at standard concentrations is added. The cells are then incubated for 72 hrs at 37°C, after which the growth medium is collected for purification of HPP. Plasmid DNA for the transfections is obtained by growing pcD(SRα), or like expression vector, containing the HPP-encoding cDNA insert in E. coli MC1061 (described by Casadaban and Cohen, J. Mol. Biol., Vol. 138, pgs. 179-207 (1980)), or like organism. The plasmid DNA is isolated from the cultures by standard techniques, e.g. Sambrook et al., Molecular Cloning: A Laboratory Manual, Second Edition (Cold Spring Harbor Laboratory, New York, 1989) or Ausubel et al (1990, cited above).

Expression in Insect Cells

HPPs may also be produced in insect cells. Expression vectors for the transformation of insect cells, and in particular, baculovirus-based expression vectors, are well known in the art. In one such system, the HPP-encoding DNA is fused upstream of an epitope tag contained within a baculovirus expression vector. *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* Sf9 cells or in Trichoplusia larvae. The HPP-encoding sequence is cloned into a nonessential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of an HPP-encoding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein coat. The recombinant viruses are then used to infect *S. frugiperda* cells or Trichoplusia larvae in which the HPP is expressed (Smith et al., J. Wol. 46:584 (1994); Engelhard E K et al., *Proc. Nat. Acad. Sci.* 91:3224-3227 (1994)). Suitable epitope tags for fusion to the HPP-encoding DNA include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including commercially available plasmids such as pVL1393 (Novagen). Briefly, the HPP-encoding DNA or the desired portion of the HPP-encoding DNA is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking restriction sites. The PCR product is then digested with the selected restriction enzymes and subcloned into an expression vector. Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGoldTM virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL), or other methods known to those of skill in the art. Virus is produced by day 4-5 of culture in Sf9 cells at 28°C, and used for further

amplifications. Procedures are performed as further described in O'Reilley et al., *BACULOVIRUS EXPRESSION VECTORS: A LABORATORY MANUAL,* Oxford University Press (1994). Extracts may be prepared from recombinant virus-infected Sf9 cells as described in Rupert et al., *Nature* 362:175-179 (1993). Alternatively, expressed epitope-tagged HPP can be purified by affinity chromatography, or for example, purification of an IgG tagged (or Fc tagged) HPP can be performed using chromatography techniques, including Protein A or protein G column chromatography.

Evaluation of Gene Expression

Gene expression may be evaluated in a sample directly, for example, by standard techniques known to those of skill in the art, e.g., Northern blotting to determine the transcription of mRNA, dot blotting (DNA or RNA), or in situ hybridization, using an appropriately labeled probe, based on the sequences provided herein. Alternatively, antibodies may be used in assays for detection of polypeptides, nucleic acids, such as specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes. Such antibodies may be labeled and the assay carried out where the duplex is bound to a surface, so that upon the formation of duplex on the surface, the presence of antibody bound to the duplex can be detected. Gene expression, alternatively, may be measured by immunohistochemical staining of cells or tissue sections and assay of cell culture or body fluids, to directly evaluate the expression of an HPP polypeptide or polynucleotide. Antibodies useful for such immunological assays may be either monoclonal or polyclonal, and may be prepared against a native sequence HPP. Protein levels may also be detected by mass spectrometry. A further method of protein detection is with retentate chromatography (including protein arrays) and surface enhanced laser desorption/ionization (SELDI) techniques.

Purification of Expressed Protein

Expressed HPP may be purified or isolated after expression, using any of a variety of methods known to those skilled in the art. The appropriate technique will vary depending upon what other components are present in the sample. Contaminant components that are removed by isolation or purification are materials that would typically interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other solutes. The purification step(s) selected will depend, for example, on the nature of the production process used and the particular HPP produced. As HPPs are secreted, they may be recovered from culture medium. Alternatively, the HPP may be recovered from host cell lysates. If membrane-bound, it can be released from the membrane using a suitable detergent solution (e.g. Triton-X 100) or by enzymatic cleavage.

Alternatively, cells employed in expression of HPP can be disrupted by various physical or chemical means, such as freeze-thaw cycling, sonication, mechanical disruption, or by use of cell lysing agents. Exemplary purification methods include, but are not limited to, ion-exchange column chromatography; chromatography using silica gel or a cation-exchange resin such as DEAE; gel filtration using, for example, Sephadex G-75; protein A Sepharose columns to remove contaminants such as IgG; chromatography using metal chelating columns to bind epitope-tagged forms of the HPP; ethanol precipitation; reverse phase HPLC; chromatofocusing; SDS-PAGE; and ammonium sulfate precipitation. Ordinarily, an isolated HPP will be prepared by at least one purification step. For example, the HPP may be purified using a standard anti-HPP antibody column. Ultrafiltration and dialysis techniques, in conjunction with protein concentration, are also useful (see, for example, Scopes, R., *PROTEIN PURIFICATION,* Springer-Verlag, New York, N.Y., 1982). The degree of purification necessary will vary depending on the use of the HPP. In some instances no purification will be necessary. Once expressed and purified as needed, the HPPs and nucleic acids of the present invention are useful in a number of applications, as detailed herein.

Assessing HPP activity

It will be appreciated that the invention further provides methods of testing the activity of or obtaining functional fragments and variants of HPPs and HPP sequences. Such methods involve providing a variant or modified HPP-encoding nucleic acid and assessing whether the encoded polypeptide displays an HPP biological activity. Encompassed is thus a method of assessing the function of an HPP comprising: (a) providing an HPP, or a biologically active fragment or homologue thereof; and (b) testing said HPP, or a biologically active fragment or homologue thereof for an HPP biological activity under conditions suitable for HPP activity. Cell free, cell-based and in vivo assays may be used to test HPP activity. For example, said assay may comprise expressing an HPP nucleic acid in a host cell, and observing HPP activity in said cell and other affected cells. In another example, an HPP, or a biologically active fragment or homologue thereof is contacted with a cell, and an HPP biological activity is observed.

HPP biological activities include: (1) circulating through the bloodstream of human individuals; (2) antigenicity, or the ability to bind an anti-HPP specific antibody; (3) immunogenicity, or the ability to generate an anti-HPP specific antibody; and (4) interaction with an HPP target molecule or adsorbant.

HPP biological activity can be assayed by any suitable method known in the art. Antigenicity and immunogenicity may be detected, for example, as described in the sections titled "Anti HPP

antibodies" and "Uses of HPP antibodies". Circulation in blood plasma may be detected as described in "Diagnostic and Prognostic Uses".

Determining the ability of the HPP to bind to or interact with an HPP target molecule can be accomplished by a method for directly or indirectly determining binding, as is common to the art. Such methods can be cell-based (e.g., such that binding to a membrane-bound HPP is detected) or cell free. Interaction of a test compound with an HPP can be detected, for example, by coupling the HPP or biologically active portion thereof with a label group such that binding of the HPP or biologically active portion thereof to its cognate target molecule can be determined by detecting the labeled HPP or biologically active portion thereof in a complex. For example, the extent of complex formation may be measured by immunoprecipitating the complex or by performing gel electrophoresis. Determining the ability of the HPP to bind to an HPP target molecule may also be accomplished using a technology such as real-time Biomolecular Interaction Analysis (BIA). Sjolander, S. and Urbaniczky, C. (1991) Anal. Chem. 63:2338-2345 and Szabo et al. (1995) Curr. Opin. Struct. Biol. 5:699-705. As used herein, "BIA" is a technology for studying biospecific interactions in real time, without labeling any of the interactants (e.g., BIAcore). Changes in the optical phenomenon of surface plasmon resonance (SPR) can be used as an indication of real-time reactions between biological molecules. Protein array methods are useful for detecting interaction. For example, one member of a receptor/ ligand pair is docked to an adsorbent, and its ability to bind the binding partner is determined in the presence of the test substance. Because of the rapidity with which adsorption can be tested, combinatorial libraries of test substances can be easily screened for their ability to modulate the interaction. In preferred methods, HPPs are docked to the adsorbent. Binding partners are preferably labeled, thus enabling detection of the interaction. Alternatively, in certain embodiments, a test substance is docked to the adsorbent. The polypeptides of the invention are exposed to the test substance and binding detected.

Anti-HPP Antibodies

The present invention provides antibodies and binding compositions specific for HPPs. Such antibodies and binding compositions include polyclonal antibodies, monoclonal antibodies, Fab and single chain Fv fragments thereof, bispecific antibodies, heteroconjugates, and humanized antibodies. Such antibodies and binding compositions may be produced in a variety of ways, including hybridoma cultures, recombinant expression in bacteria or mammalian cell cultures, and recombinant expression in transgenic animals. There is abundant guidance in the literature for selecting a particular production methodology, e.g. Chadd and Chamow, Curr. Opin. Biotechnol., 12: 188-194 (2001).

The choice of manufacturing methodology depends on several factors including the antibody structure desired, the importance of carbohydrate moieties on the antibodies, ease of culturing and purification, and cost. Many different antibody structures may be generated using standard expression technology, including full-length antibodies, antibody fragments, such as Fab and Fv fragments, as well as chimeric antibodies comprising components from different species. Antibody fragments of small size, such as Fab and Fv fragments, having no effector functions and limited pharmokinetic activity may be generated in a bacterial expression system. Single chain Fv fragments are highly selective for in vivo tumors, show good tumor penetration and low immunogenicity, and are cleared rapidly from the blood, e.g. Freyre et al, J. Biotechnol., 76: 157-163 (2000). Thus, such molecules are desirable for radioimmunodetection.

Polyclonal Antibodies

The anti-HPP antibodies of the present invention may be polyclonal antibodies. Such polyclonal antibodies can be produced in a mammal, for example, following one or more injections of an immunizing agent, and preferably, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected into the mammal by a series of subcutaneous or intraperitoneal injections. The immunizing agent may include HPPs or a fusion protein thereof. It may be useful to conjugate the antigen to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include, but are not limited to, keyhole limpet hemocyanin (KLH), methylated bovine serum albumin (mBSA), bovine serum albumin (BSA), Hepatitis B surface antigen, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Adjuvants include, for example, Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicoryno-mycolate). The immunization protocol may be determined by one skilled in the art based on standard protocols or by routine experimentation.

Alternatively, a crude protein preparation which has been enriched for an HPP or a portion thereof can be used to generate antibodies. Such proteins, fragments or preparations are introduced into the non-human mammal in the presence of an appropriate adjuvant. If the serum contains polyclonal antibodies to undesired epitopes, the polyclonal antibodies are purified by immunoaffinity chromatography.

Effective polyclonal antibody production is affected by many factors related both to the antigen and the host species. Also, host animals vary in response to site of inoculations and dose, with both inadequate and excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appear to be most reliable. Techniques for

producing and processing polyclonal antisera are known in the art, see for example, Mayer and Walker (1987). An effective immunization protocol for rabbits can be found in Vaitukaitis, J. et al. J. Clin. Endocrinol. Metab. 33:988-991(1971). Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, O. et al., Chap. 19 in: Handbook of Experimental Immunology D. Wier (ed) Blackwell (1973). Plateau concentration of antibody is usually in the range of 0.1 to 0.2 mg/ml of serum. Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as described, for example, by Fisher, D., Chap. 42 in: Manual of Clinical Immunology, 2d Ed. (Rose and Friedman, Eds.) Amer. Soc. For Microbiol., Washington, D. C. (1980).

Monoclonal Antibodies

Alternatively, the anti-HPP antibodies may be monoclonal antibodies. Monoclonal antibodies may be produced by hybridomas, wherein a mouse, hamster, or other appropriate host animal, is immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent, e.g. Kohler and Milstein, Nature 256:495 (1975). The immunizing agent will typically include the HPP or a fusion protein thereof and optionally a carrier. Alternatively, the lymphocytes may be immunized in vitro. Generally, spleen cells or lymph node cells are used if non-human mammalian sources are desired, or peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired. The lymphocytes are fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to produce a hybridoma cell, e.g. Goding, *MONOCLONAL ANTIBODIES: PRINCIPLES AND PRACTICE,* Academic Press, pp. 59-103 (1986); Liddell and Cryer, A Practical Guide to Monoclonal Antibodies (John Wiley & Sons, New York, 1991); Malik and Lillenoj, Editors, Antibody Techniques (Academic Press, New York, 1994). In general, immortalized cell lines are transformed mammalian cells, for example, myeloma cells of rat, mouse, bovine or human origin. The hybridoma cells are cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine (HAT), substances which prevent the growth of HGPRT-deficient cells. Preferred immortalized cell lines are those that fuse efficiently, support stable high level production of antibody, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine or human myeloma lines, which can be obtained,

for example, from the American Type Culture Collection (ATCC), Rockville, MD. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies, e.g. Kozbor, J. Immunol. 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, pp. 51-63 (1987).

The culture medium (supernatant) in which the hybridoma cells are cultured can be assayed for the presence of monoclonal antibodies directed against an HPP. Preferably, the binding specificity of monoclonal antibodies present in the hybridoma supernatant is determined by immunoprecipitation or by an in vitro binding assay, such as radio-immunoassay (RIA) or Enzyme-Linked Immuno Sorbent Assay (ELISA). Appropriate techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, *Anal. Biochem.* 107:220 (1980). After the desired antibody-producing hybridoma cells are identified, the cells may be cloned by limiting dilution procedures and grown by standard methods (Goding, 1986, *supra*). Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells may be grown in vivo as ascites in a mammal. The monoclonal antibodies secreted by selected clones may be isolated or purified from the culture medium or ascites fluid by immunoglobulin purification procedures routinely used by those of skill in the art such as, for example, protein A-Sepharose, hydroxyl-apatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies may also be made by recombinant DNA methods, such as those described in U.S. Pat. No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be isolated from the HPP-specific hybridoma cells and sequenced, e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies. Once isolated, the DNA may be inserted into an expression vector, which is then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also may be modified, for example, by substituting the coding sequence for the murine heavy and light chain constant domains for the homologous human sequences (Morrison et al., *Proc. Nat. Acad. Sci.* 81:6851-6855 (1984); Neuberger et al., *Nature* 312:604-608 (1984); Takeda et al., *Nature* 314:452-454 (1985)), or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. The non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody. The antibodies may also be

monovalent antibodies. Methods for preparing monovalent antibodies are well known in the art. For example, in vitro methods are suitable for preparing monovalent antibodies. Digestion of antibodies to produce fragments thereof, particularly, Fab fragments, can be accomplished using routine techniques known in the art.

Antibodies and antibody fragments characteristic of hybridomas of the invention can also be produced by recombinant means by extracting messenger RNA, constructing a cDNA library, and selecting clones which encode segments of the antibody molecule. The following are exemplary references disclosing recombinant techniques for producing antibodies: Wall et al., Nucleic Acids Research, Vol. 5, pgs. 3113-3128 (1978); Zakut et al., Nucleic Acids Research, Vol. 8, pgs. 3591-3601 (1980); Cabilly et al., Proc. Natl. Acad. Sci., Vol. 81, pgs. 3273-3277 (1984); Boss et al., Nucleic Acids Research, Vol. 12, pgs. 3791-3806 (1984); Amster et al., Nucleic Acids Research, Vol. 8, pgs. 2055-2065 (1980); Moore et al., U.S. Patent 4,642,334; Skerra et al, Science, Vol. 240, pgs. 1038-1041(1988); Huse et al, Science, Vol. 246, pgs. 1275-1281 (1989); and U.S. patents 6,054,297; 5,530,101; 4,816,567; 5,750,105; and 5,648,237; which patents are incorporated by reference. In particular, such techniques can be used to produce interspecific monoclonal antibodies, wherein the binding region of one species is combined with non-binding region of the antibody of another species to reduce immunogenicity, e.g. Liu et al., Proc. Natl. Acad. Sci., Vol. 84, pgs. 3439-3443 (1987), and patents 6,054,297 and 5,530,101. Preferably, recombinantly produced Fab and Fv fragments are expressed in bacterial host systems. Preferably, full-length antibodies are produced by mammalian cell culture techniques. More preferably, full-length antibodies are expressed in Chinese Hamster Ovary (CHO) cells or NSO cells.

Both polyclonal and monoclonal antibodies can be screened by ELISA. As in other solid phase immunoassays, the test is based on the tendency of macromolecules to adsorb nonspecifically to plastic. The irreversibility of this reaction, without loss of immunological activity, allows the formation of antigen-antibody complexes with a simple separation of such complexes from unbound material. To titrate anti-peptide serum, peptide conjugated to a carrier different from that used in immunization is adsorbed to the wells of a 96-well microtiter plate. The adsorbed antigen is then allowed to react in the wells with dilutions of anti-peptide serum. Unbound antibody is washed away, and the remaining antigen-antibody complexes are allowed to react with an antibody specific for the IgG of the immunized animal. This second antibody is conjugated to an enzyme such as alkaline phosphatase. A visible colored reaction produced when the enzyme substrate is added indicates which wells have bound antipeptide antibodies. The use of spectrophotometer readings allows better quantification of the amount of peptide-specific antibody bound. High-titer antisera yield a linear

titration curve between 10^{-3} and 10^{-5} dilutions.

HPP peptide carriers

The invention includes immunogens derived from HPPs, and immunogens comprising conjugates between carriers and peptides of the invention. The term immunogen as used herein refers to a substance which is capable of causing an immune response. The term carrier as used herein refers to any substance which when chemically conjugated to a peptide of the invention permits a host organism immunized with the resulting conjugate to generate antibodies specific for the conjugated peptide. Carriers include red blood cells, bacteriophages, proteins, or synthetic particles such as agarose beads. Preferably, carriers are proteins, such as serum albumin, gamma-globulin, keyhole limpet hemocyanin (KLH), thyroglobulin, ovalbumin, or fibrinogen.

The general technique of linking synthetic peptides to a carrier is described in several references, e.g. Walter and Doolittle, "Antibodies Against Synthetic Peptides," in Setlow et al., eds., Genetic Engineering, Vol. 5, pgs. 61-91 (Plenum Press, N.Y., 1983); Green et al. Cell, Vol. 28, pgs. 477-487 (1982); Lerner et al., Proc. Natl. Acad. Sci., Vol. 78, pgs. 3403-3407 (1981); Shimizu et al., U.S. Patent 4,474,754; and Ganfield et al., U.S. Patent 4,311,639. Accordingly, these references are incorporated by reference. Also, techniques employed to link haptens to carriers are essentially the same as the above-referenced techniques, e.g. chapter 20 in Tijssen, Practice and Theory of Enzyme Immunoassays (Elsevier, New York, 1985). The four most commonly used schemes for attaching a peptide to a carrier are (1) glutaraldehyde for amino coupling, e.g. as disclosed by Kagan and Glick, in Jaffe and Behrman, eds. Methods of Hormone Radioimmunoassay, pgs. 328-329 (Academic Press, N.Y., 1979), and Walter et al. Proc. Natl. Acad. Sci., Vol. 77, pgs. 5197-5200 (1980); (2) water-soluble carbodiimides for carboxyl to amino coupling, e.g. as disclosed by Hoare et al., J. Biol. Chem., Vol. 242, pgs. 2447-2453 (1967); (3) bis-diazobenzidine (BDB) for tyrosine to tyrosine sidechain coupling, e.g. as disclosed by Bassiri et al., pgs. 46-47, in Jaffe and Behrman, eds. (cited above), and Walter et al. (cited above); and (4) maleimidobenzoyl-N-hydroxysuccinimide ester (MBS) for coupling cysteine (or other sulfhydryls) to amino groups, e.g. as disclosed by Kitagawa et al., J. Biochem. (Tokyo), Vol. 79, pgs. 233-239 (1976), and Lerner et al. (cited above). A general rule for selecting an appropriate method for coupling a given peptide to a protein carrier can be stated as follows: the group involved in attachment should occur only once in the sequence, preferably at the appropriate end of the segment. For example, BDB should not be used if a tyrosine residue occurs in the main part of a sequence chosen for its potentially antigenic character. Similarly, centrally located lysines rule out the glutaraldehyde method, and the occurrences of aspartic and glutamic acids

frequently exclude the carbodiimide approach. On the other hand, suitable residues can be positioned at either end of chosen sequence segment as attachment sites, whether or not they occur in the "native" protein sequence. Internal segments, unlike the amino and carboxy termini, will differ significantly at the "unattached end" from the same sequence as it is found in the native protein where the polypeptide backbone is continuous. The problem can be remedied, to a degree, by acetylating the α-amino group and then attaching the peptide by way of its carboxy terminus. The coupling efficiency to the carrier protein is conveniently measured by using a radioactively labeled peptide, prepared either by using a radioactive amino acid for one step of the synthesis or by labeling the completed peptide by the iodination of a tyrosine residue. The presence of tyrosine in the peptide also allows one to set up a sensitive radioimmune assay, if desirable. Therefore, tyrosine can be introduced as a terminal residue if it is not part of the peptide sequence defined by the native polypeptide.

Preferred carriers are proteins, and preferred protein carriers include bovine serum albumin, myoglobulin, ovalbumin (OVA), keyhole limpet hemocyanin (KLH), or the like. Peptides can be linked to KLH through cysteines by MBS as disclosed by Liu et al., Biochemistry, Vol. 18, pgs. 690-697 (1979). The peptides are dissolved in phosphate-buffered saline (pH 7.5), 0.1 M sodium borate buffer (pH 9.0) or 1.0 M sodium acetate buffer (pH 4.0). The pH for the dissolution of the peptide is chosen to optimize peptide solubility. The content of free cysteine for soluble peptides is determined by Ellman's method, Ellman, Arch. Biochem. Biophys., Vol. 82, pg. 7077 (1959). For each peptide, 4 mg KLH in 0.25 ml of 10 mM sodium phosphate buffer (pH 7.2) is reacted with 0.7 mg MBS (dissolved in dimethyl formamide) and stirred for 30 min at room temperature. The MBS is added dropwise to ensure that the local concentration of formamide is not too high, as KLH is insoluble in >30% formamide. The reaction product, KLH-MBS, is then passed through Sephadex G-25 equilibrated with 50 mM sodium phosphate buffer (pH 6.0) to remove free MBS, KLH recovery from peak fractions of the column eluate (monitored by OD280) is estimated to be approximately 80%. KLH-MBS is then reacted with 5 mg peptide dissolved in 1 ml of the chosen buffer. The pH is adjusted to 7-7.5 and the reaction is stirred for 3 hr at room temperature. Coupling efficiency is monitored with radioactive peptide by dialysis of a sample of the conjugate against phosphate-buffered saline, and may range from 8% to 60%. Once the peptide-carrier conjugate is available, polyclonal or monoclonal antibodies are produced by standard techniques, e.g. as disclosed by Campbell, Monoclonal Antibody Technology (Elsevier, New York, 1984); Hurrell, ed. Monoclonal Hybridoma Antibodies: Techniques and Applications (CRC Press, Boca Raton, FL, 1982); Schreier et al. Hybridoma Techniques (Cold Spring Harbor Laboratory, New York, 1980); U.S. Patent

4,562,003.

Humanized Antibodies

The anti-HPP antibodies of the invention may further comprise humanized antibodies or human antibodies. The term "humanized antibody" refers to humanized forms of non-human (e.g., murine) antibodies that are chimeric antibodies, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab'), or other antigen-binding partial sequences of antibodies) which contain some portion of the sequence derived from non-human antibody. Humanized antibodies include human immunoglobulins in which residues from a complementary determining region (CDR) of the human immunoglobulin are replaced by residues from a CDR of a non-human species such as mouse, rat or rabbit having the desired binding specificity, affinity and capacity. In general, the humanized antibody will comprise substantially all of at least one, and generally two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin (Jones et al., *Nature* 321:522-525 (1986) and Presta, *Curr. Op. Struct. Biol. 2:593-596* (1992)). Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acids introduced into it from a source which is non-human in order to more closely resemble a human antibody, while still retaining the original binding activity of the antibody. Methods for humanization of antibodies are further detailed in Jones et al., *Nature* 321:522-525 (1986); Riechmann et al., *Nature* 332:323-327 (1988); and Verhoeyen et al., *Science* 239:1534-1536 (1988). Such "humanized" antibodies are chimeric antibodies in that substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species.

Heteroconjugate Antibodies

Heteroconjugate antibodies which comprise two covalently joined antibodies, are also within the scope of the present invention. Heteroconjugate antibodies may be prepared in vitro using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins may be prepared using a disulfide exchange reaction or by forming a thioether bond.

Bispecific Antibodies

Bispecific antibodies have binding specificities for at least two different antigens. Such

antibodies are monoclonal, and preferably human or humanized. One of the binding specificities of a bispecific antibody of the present invention is for an HPP, and the other one is preferably for a cell-surface protein or receptor or receptor subunit. Methods for making bispecific antibodies are known in the art, and in general, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs in hybridoma cells, where the two heavy chains have different specificities, e.g. Milstein and Cuello, *Nature 305:537-539* (1983). Given that the random assortment of immunoglobulin heavy and light chains results in production of potentially ten different antibody molecules by the hybridomas, purification of the correct molecule usually requires some sort of affinity purification, e.g. affinity chromatography.

Uses of HPP antibodies

HPP antibodies are preferably specific for the HPPs of the invention and, as such, do not bind peptides derived from other proteins with high affinity. As used herein, the term "heavy chain variable region" means a polypeptide (1) which is from 110 to 125 amino acids in length, and (2) whose amino acid sequence corresponds to that of a heavy chain of an antibody of the invention, starting from the heavy chain's N-terminal amino acid. Likewise, the term "light chain variable region" means a polypeptide (1) which is from 95 to 115 amino acids in length, and (2) whose amino acid sequence corresponds to that of a light chain of an antibody of the invention, starting from the light chain's N-terminal amino acid. As used herein the term "monoclonal antibody" refers to homogeneous populations of immunoglobulins which are capable of specifically binding to HPPs.

The use of antibody fragments is also well known, e.g. Fab fragments: Tijssen, Practice and Theory of Enzyme Immunoassays (Elsevier, Amsterdam, 1985); and Fv fragments: Hochman et al. Biochemistry, Vol. 12, pgs. 1130-1135 (1973), Sharon et al., Biochemistry, Vol. 15, pgs. 1591-1594 (1976) and Ehrlich et al., U.S. Patent 4,355,023; and antibody half molecules: Auditore- Hargreaves, U.S. Patent 4,470,925.

Preferably, monoclonal antibodies, Fv fragments, Fab fragments, or other binding compositions derived from monoclonal antibodies of the invention have a high affinity to HPPs. The affinity of monoclonal antibodies and related molecules to HPPs may be measured by conventional techniques including plasmon resonance, ELISA, or equilibrium dialysis. Affinity measurement by plasmon resonance techniques may be carried out, for example, using a BIAcore 2000 instrument (Biacore AB, Uppsala, Sweden) in accordance with the manufacturer's recommended protocol. Preferably, affinity is measured by ELISA, as described in U.S. patent 6,235,883, for example. Preferably, the dissociation constant between HPPs and monoclonal antibodies of the invention is less

than 10^{-5} molar. More preferably, such dissociation constant is less than 10^{-8} molar; still more preferably, such dissociation constant is less than 10^{-9} molar; and most preferably, such dissociation constant is in the range of 10^{-9} to 10^{-11} molar.

The antibodies of the present invention are useful for detecting HPPs. Such detection methods are advantageously applied to diagnosis of HPP-related disorders. The antibodies of the invention may be used in most assays involving antigen-antibody reactions. The assays may be homogeneous or heterogeneous. In a homogeneous assay approach, the sample can be a biological sample or fluid such as serum, urine, whole blood, lymphatic fluid, plasma, saliva, cells, tissue, and material secreted by cells or tissues cultured in vitro. The sample can be pretreated if necessary to remove unwanted materials. The immunological reaction usually involves the specific antibody, a labeled analyte, and the sample suspected of containing the antigen. The signal arising from the label is modified, directly or indirectly, upon the binding of the antibody to the labeled analyte. Both immunological reaction and detection of the extent thereof are carried out in a homogeneous solution. Immunochemical labels which may be employed include free radicals, fluorescent dyes, enzymes, bacteriophages, coenzymes, and so forth.

In a heterogeneous assay approach, the reagents are usually the sample, the specific antibody, and means for producing a detectable signal. The specimen is generally placed on a support, such as a plate or a slide, and contacted with the antibody in a liquid phase. The support is then separated from the liquid phase and either the support phase or the liquid phase is examined for a detectable signal employing means for producing such signal or signal producing system. The signal is related to the presence of the antigen in the sample. Means for producing a detectable signal includes the use of radioactive labels, fluorescent compounds, enzymes, and so forth. Exemplary heterogeneous immunoassays are the radioimmunoassay, immunofluorescence methods, enzyme-linked immunoassays, and the like.

For a more detailed discussion of the above immunoassay techniques, see "Enzyme-Immunoassay," by Edward T. Maggio, CRC Press, Inc., Boca Raton, Fla., 1980. See also, for example, U.S. Pat. Nos. 3,690,834; 3,791,932; 3,817,837; 3,850,578; 3,853,987; 3,867,517; 3,901,654; 3,935,074; 3,984,533; 3,966,345; and 4,098,876, which listing is not intended to be exhaustive. Methods for conjugating labels to antibodies and antibody fragments are well known in the art. Such methods may be found in U.S. Pat. Nos. 4,220,450; 4,235,869; 3,935,974; and 3,966,345. Another example of a technique in which the antibodies of the invention may be employed is immunoperoxidase labeling. (Sternberger, Immunocytochemistry (1979) pp. 104-169).

One embodiment of an assay employing an antibody of the present invention involves the use

of a surface to which the monoclonal antibody of the invention is attached. The underlying structure of the surface may take different forms, have different compositions and may be a mixture of compositions or laminates or combinations thereof. The surface may assume a variety of shapes and forms and may have varied dimensions, depending on the manner of use and measurement. Illustrative surfaces may be pads, beads, discs, or strips which may be flat, concave or convex. Thickness is not critical, generally being from about 0.1 to 2 mm thick and of any convenient diameter or other dimensions. The surface typically will be supported on a rod, tube, capillary, fiber, strip, disc, plate, cuvette and will typically be porous and polyfunctional or capable of being polyfunctionalized so as to permit covalent binding of an antibody and permit bonding of other compounds which form a part of a means for producing a detectable signal. A wide variety of organic and inorganic polymers, both natural and synthetic, and combinations thereof, may be employed as the material for the solid surface. Illustrative polymers include polyethylene, polypropylene, poly(4-methylbutene), polystyrene, polymethracrylate, poly(ethylene terephthalate), rayon, nylon, poly(vinyl butyrate), silicones, polyformaldehyde, cellulose, cellulose acetate, nitrocellulose, and latex. Other surfaces include paper, glasses, ceramics, metals, metaloids, semiconductor materials, cements, silicates or the like. Also included are substrates that form gels, gelatins, lipopolysaccharides, silicates, agarose and polyacrylamides or polymers which form several aqueous phases such as dextrans, polyalkylene glycols (alkylene of 2 to 3 carbon atoms) or surfactants such as phospholipids. The binding of the antibody to the surface may be accomplished by well known techniques, commonly available in the literature (see, for example, "Immobilized Enzymes," Ichiro Chibata, Press, New York (1978) and Cuatrecasas, J. Bio. Chem., 245: 3059 (1970)). In carrying out the assay in accordance with this aspect of the invention, the sample is mixed with aqueous medium and the medium is contacted with the surface having an antibody bound thereto. Labels may be included in the aqueous medium, either concurrently or added subsequently so as to provide a detectable signal associated with the surface. The means for producing the detectable signal can involve the incorporation of a labeled analyte or it may involve the use of a second monoclonal antibody having a label conjugated thereto. Separation and washing steps will be carried out as needed. The signal detected is related to the presence of HPP in the sample. It is within the scope of the present invention to include a calibration on the same support. A particular embodiment of an assay in accordance with the present invention, by way of illustration and not limitation, involves the use of a support such as a slide or a well of a petri dish. The technique involves fixing the sample to be analyzed on the support with an appropriate fixing material and incubating the sample on the slide with a monoclonal antibody. After washing with an appropriate buffer such as, for example, phosphate buffered saline, the support is contacted with a

labeled specific binding partner for the antibody. After incubation as desired, the slide is washed a second time with an aqueous buffer and the determination is made of the binding of the labeled monoclonal antibody to the antigen. If the label is fluorescent, the slide may be covered with a fluorescent antibody mounting fluid on a cover slip and then examined with a fluorescent microscope to determine the extent of binding. On the other hand, the label can be an enzyme conjugated to the monoclonal antibody and the extent of binding can be determined by examining the slide for the presence of enzyme activity, which may be indicated by the formation of a precipitate, color, etc.

A particular example of an assay utilizing the present antibodies is a double determinant ELISA assay. A support such as, e.g., a glass or vinyl plate, is coated with an antibody specific for HPP by conventional techniques. The support is contacted with the sample suspected of containing HPP, usually in aqueous medium. After an incubation period from 30 seconds to 12 hours, the support is separated from the medium, washed to remove unbound HPP with, for example, water or an aqueous buffered medium, and contacted with an antibody specific for HPP, again usually in aqueous medium. The antibody is labeled with an enzyme directly or indirectly such as, e.g., horseradish peroxidase or alkaline phosphatase. After incubation, the support is separated from the medium, and washed as above. The enzyme activity of the support or the aqueous medium is determined. This enzyme activity is related to the amount of HPP in the sample.

Another antibody-utilizing method of detection includes retentate chromotography methods, as described herein. In this case, the adsorbant is an antibody. Preferably, more than one antibody specific for more than one HPP of the invention is included on a surface or substrate.

The invention also includes kits, e.g., diagnostic assay kits, for carrying out the methods disclosed above. In one embodiment, the kit comprises in packaged combination (a) a monoclonal antibody more specifically defined above and (b) a conjugate of a specific binding partner for the above monoclonal antibody and a label capable of producing a detectable signal. The reagents may also include ancillary agents such as buffering agents and protein stabilizing agents, e.g., polysaccharides and the like. The kit may further include, where necessary, other members of the signal producing system of which system the label is a member, agents for reducing background interference in a test, control reagents, apparatus for conducting a test, and the like. In another embodiment, the diagnostic kit comprises a conjugate of monoclonal antibody of the invention and a label capable of producing a detectable signal. Ancillary agents as mentioned above may also be present.

Further, an anti-HPP antibody (e.g., monoclonal antibody) can be used to isolate HPPs by standard techniques, such as affinity chromatography or immunoprecipitation. For example, an anti-

HPP antibody can facilitate the purification of natural HPPs from cells and of recombinantly produced HPP expressed in host cells. Moreover, an anti-HPP antibody can be used to isolate HPP to aid in detection of low concentrations of HPP (e.g., in plasma, cellular lysate or cell supernatant) or in order to evaluate the abundance and pattern of expression of the HPP. Anti-HPP antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (i.e., physically linking) the antibody to a label group.

Detection Using Protein Arrays

Detection and purification of the polypeptides of the invention may be accomplished using retentate chromatography (preferably, protein arrays or chips), as described by U.S. Patent 6225027 and U.S. Patent Application 20010014461. Briefly, retentate chromatography describes methods in which polypeptides (and/ or other sample components) are retained on an adsorbent (e.g., array or chip) and subsequently detected. Such methods involve (1) selectively adsorbing polypeptides from a sample to a substrate under a plurality of different adsorbent/eluant combinations ("selectivity conditions") and (2) detecting the retention of adsorbed polypeptides by desorption spectrometry (e.g., by mass spectrometry). "Desorption spectrometry" refers to a method of detecting a substance (e.g., polypeptide) in which the substance is exposed to energy which desorbs it from a stationary phase into a gas phase, and the desorbed substance or a distinguishable portion of it is directly detected by a detector, without an intermediate capture on a second stationary phase. In conventional chromatographic methods, polypeptides are eluted off of the adsorbent prior to detection. The coupling of adsorption chromatography with detection by desorption spectrometry provides extraordinary sensitivity, the ability to rapidly analyze retained components with a variety of different selectivity conditions, and parallel processing of components adsorbed to different sites (i.e., "affinity sites" or "spots") on the array under different elution conditions.

A preferred embodiment provides adsorbents, either chemical (e.g., ion-affinity or hydrophobic substances) or biospecific (e.g., antibodies or antigen-binding fragments thereof), developed to detect a specific polypeptide, preferably an HPP. In certain embodiments, a substrate has an array of adsorbent spots selected for a combination of polypeptides, e.g. as diagnostic markers. As few as two and as many as 10, 100, 1000, or more adsorbents can be coupled to a single substrate. The size of the adsorbent site may be varied, depending on experimental design and purpose. However, it does not need to be larger than the diameter of the impinging energy source (e.g., laser spot diameter). The spots can be made of the same or different adsorbents. In some cases, it is

advantageous to provide the same adsorbent at multiple locations on the substrate to permit evaluation against a plurality of different eluants or so that the bound polypeptide can be preserved for future use or reference, perhaps in secondary processing. By providing a substrate with a plurality of different adsorbents, it is possible to utilize the plurality of binding characteristics provided by the combination of different adsorbents with respect to a single sample (e.g., plasma sample) and thereby bind and detect a wider variety of different polypeptides (preferably HPPs). The use of a plurality of different adsorbents on a substrate for evaluation of a single sample is essentially equivalent to concurrently conducting multiple chromatographic experiments, each with a different chromatography column, but the present method has the advantage of requiring only a single system.

When the substrate includes a plurality of adsorbents, it is particularly useful to provide the adsorbents in predetermined addressable locations. By providing the adsorbents in predetermined addressable locations, it is possible to wash an adsorbent at a first predetermined addressable location with a first eluant and to wash an adsorbent at a second predetermined addressable location with a second eluant. In this manner, the binding characteristics of a single adsorbent for its specified polypeptide can be evaluated in the presence of multiple eluants which each selectively modify each set of adsorbant-polypeptide binding characteristics.

Retentate chromotography may be used in a combinatorial separation method that includes separation and detection of multiple polypeptides in parallel. The method comprises the steps of a) exposing a sample (e.g., a biological fluid such as plasma) to at least two different selectivity conditions, each selectivity condition defined by the combination of an adsorbent and an eluant, to allow retention of a polypeptide by the adsorbent; and b) detecting retained polypeptide under the different selectivity conditions by desorption spectrometry. Each different selectivity condition is defined at a different predetermined, addressable location for parallel processing. The method comprises the steps of i) exposing a sample to a first selectivity condition at a defined location to allow retention of a polypeptide by an adsorbent; ii) detecting retained polypeptide under the first selectivity condition by desorption spectrometry; iii) washing the adsorbent under a second, different selectivity condition at the defined location to allow retention of a polypeptide to the adsorbent at that location; and iv) detecting retained polypeptides under the second selectivity condition by desorption spectrometry.

Polypeptides may be detected by gas phase ion spectrometry, SELDI, or mass spectrometry techniques detailed herein. "Gas phase ion spectrometry" refers to a method of employing an ionization source to generate gas phase ions from a substance presented on a surface and detecting the gas phase ions with a gas phase ion spectrometer. "Surface-enhanced laser desorption/ionisation" or

"SELDI" is a method of gas phase ion spectrometry in which the substance-presenting surface plays an active role in desorption and ionization process. SELDI technology is described in, e.g., U.S. Patents 5,719,060 and 6,225,047 (Hutchens and Yip).

These methods are useful for: combinatorial, biochemical separation and purification of the HPPs; study of differential gene expression; and detection of differences in protein levels between samples (e.g., for diagnosis). WO 03/019193 (Ciphergen) describes the use of such methods for detection of specific kidney disease markers in a fluid sample. A similar approach is taken by Yip and Lomas (Technol Cancer Res Treat, 2002, 1:273-80) to detect cancer-related polypeptides. HPPs of the invention or HPP-binding substances are preferably attached to a label group, and thus directly detected, enabling simultaneous transmission of two or more signals from the same "circuit" (i.e., addressable "chip" location) during a single unit operation. A preferred embodiment of the invention encompasses use of retentate chromotography to identify at least one HPP in a sample, preferably plasma.

A variation of microchip-based detection utilizes electrophoresis, as described by Chen, et al. (Anal Chem 2002; 74:5146-53). In this method, a flow-through sampling chip is applied to immunoseparation, protein purification, concentration, and detection purposes. This device uses hydrodynamic pressure to drive the sample flow, and a gating voltage is applied to the electrophoretic channel on the microchip. Using this device, the wash/elution step can be integrated on-line with electrophoretic separation and detection on the microchip. Moreover, the electrical field-free bed ensures that protein-adsorbant interaction will not be affected by the electric field during the wash/elution step.

Detection of HPPs by mass spectrometry

In accordance with the present invention, any instrument, method, process, etc. can be utilized to determine the identity and abundance of proteins in a sample. A preferred method of obtaining identity is by mass spectrometry, where protein molecules in a sample are ionized and then the resultant mass and charge of the protein ions are detected and determined.

To use mass spectrometry to analyze proteins, it is preferred that the protein be converted to a gas-ion phase. Various methods of protein ionization are useful, including, e.g., fast ion bombardment (FAB), plasma desorption, laser desorption, thermal desorption, preferably, electrospray ionization (ESI) and matrix-assisted laser desorption/ionization (MALDI). Many different mass analyzers are available for peptide and protein analysis, including, but not limited to, Time-of-Flight (TOF), ion trap (ITMS), Fourier transform ion cyclotron (FTMS), quadrupole ion trap, and sector (electric and/or

magnetic) spectrometers. See, e.g., U.S. Pat. No. 5,572,025 for an ion trap MS. Mass analyzers can be used alone, or in combination with other mass analyzers in tandem mass spectrometers. In the latter case, a first mass analyzer can be use to separate the protein ions (precursor ion) from each other and determine the molecular weights of the various protein constituents in the sample. A second mass analyzer can be used to analyze each separated constituents, e.g., by fragmenting the precursor ions into product ions by using, e.g. an inert gas. Any desired combination of mass analyzers can be used, including, e.g., triple quadrupoles, tandem time-of-flights, ion traps, and/or combinations thereof.

Different kinds of detectors can be used to detect the protein ions. For example, destructive detectors can be utilized, such as ion electron multipliers or cryogenic detectors (e.g., U.S. Patent 5,640,010). Additionally, non-destructive detectors can be used, such as ion traps which are used as ion current pick-up devices in quadrupole ion trap mass analyzers or FTMS.

For MALDI-TOF, a number of sample preparation methods can be utilized including, dried droplet (Karasand Hillenkamp, Anal. Chem., 60:2299-2301, 1988), vacuum-drying (Winberger et al., In Proceedings of the 41st ASMS Conference on Mass Spectrometry and Allied Topics, San Francisco, May 31-June 4, 1993, pp. 775a-b), crush crystals (Xiang et al., Rapid Comm. Mass Spectrom., 8:199-204,1994), slow crystal growing (Xiang et al., Org. Mass Spectrom, 28:1424-1429, 1993); active film (Mock et al., Rapid Comm. Mass Spectrom.,6:233-238, 1992; Bai et al., Anal. Chem., 66:3423-3430, 1994), pneumatic spray (Kochling et al., Proceedings of the 43rd ASMS Conference on Mass Spectrometry and Allied Topics; Atlanta, GA, May 21-26, 1995, p1225); electrospray (Hensel et al., Proceedings of the 43rd ASMS Conference on Mass Spectrometry and Allied Topics; Atlanta, GA, May 21 -26, 1995, p947); fast solvent evaporation (Vorm et al., Anal. Chem., 66:3281-3287, 1994); sandwich (Li et al., J. Am. Chem. Soc., 11 8:11662-11663,1996); and two-layer methods (Dal et al., Anal. Chem., 71:1087-1091, 1999). See also, e.g., Liang et al., Rapid Commun. Mass Spectrom., 10: 1219-1226, 1996; van Adrichemet al., Anal. Chem., 70:923-930, 1998.

For MALDI analysis, samples are prepared as solid-state co-crystals or thin films by mixing them with an energy absorbing compound or colloid (the matrix) in the liquid phase, and ultimately drying the solution to the solid state upon the surface of an inert probe. In some cases an energy absorbing molecule (EAM) is an integral component of the sample presenting surface. Regardless of EAM application strategy, the probe contents are allowed to dry to the solid state prior to introduction into the laser desorption/ionization time-of-flight mass spectrometer (LDIMS).

Ion detection in TOF mass spectrometry is typically achieved with the use of electro-emissive detectors such as electron multipliers (EMP) or microchannel plates (MCP). Both of these devices

function by converting primary incident charged particles into a cascade of secondary, tertiary, quaternary, etc. electrons. The probability of secondary electrons being generated by the impact of a single incident charged particle can be taken to be the ion-to-electron conversion efficiency of this charged particle (or more simply, the conversion efficiency). The total electron yield for cascading events when compared to the total number of incident charged particles is typically described as the detector gain. Because generally the overall response time of MCPs is far superior to that of EMPs, MCPs are the preferred electro-emissive detector for enhancing mass/charge resolving power. However, EMPs function well for detecting ion populations of disbursed kinetic energies, where rapid response time and broad frequency bandwidth are not necessary.

In a preferred aspect, for the analysis of digested proteins, a liquid-chromatography tandem mass spectrometer (LC-TMS) is used. This system provides an additional stage of sample separation via use of a liquid chromatograph followed by tandem mass spectrometry.

Electrospray ionization (ESI) and MALDI are commonly used ionization techniques for interfacing capillary electrophoresis (CE) to MS (Moini, M., Anal Bioanal Chem, 2002; 373:466-80). CE has the advantage of high sensitivity and separation efficiency. The high concentration detection limit of CE has been addressed by development of sample concentration and sample focusing methods. In addition, a wide variety of techniques such as capillary zone electrophoresis, capillary isoelectric focusing, and on-column transient isotachophoresis have now been interfaced to MS. Deterding, et al. (Electrophoresis 2002; 23:2296-305) describe successful application of CE-MS techniques for identification of apolipoprotein species from plasma samples. Thus, it is envisioned that these methods are similarly applied to detect HPPs, in particular, in human plasma samples.

In preferred aspects, a protein eluted from a column according to the system described in Example 1 is analyzed using both MS and MS-MS analysis. For example, a small portion of intact proteins eluting from RP2 may be diverted to online detection using LC-ESI MS. The proteins are aliquoted on a number of plates allowing digestion or not with trypsin, preparation for MALDI-MS as well as for ESI-MS, as well as preparation of the MALDI plates with different matrices. The methods thus allow, in addition to information on intact mass, to conduct an analysis by both peptide mass fingerprinting and MS-MS techniques.

The methods described herein of separating and fractionating proteins provide individual proteins or fractions containing small numbers of distinct proteins. These proteins can be identified by mass spectral determination of the molecular masses of the protein and peptides resulting from the fragmentation thereof. Making use of available information in protein sequence databases, a comparison can be made between proteolytic peptide mass patterns generated *in silico,* and

experimentally observed peptide masses. A "hit-list" can be compiled, ranking candidate proteins in the database, based on (among other criteria) the number of matches between the theoretical and experimental proteolytic fragments. Several Web sites are accessible that provide software for protein identification on-line, based on peptide mapping and sequence database search strategies (e.g., http://www.expasy.ch). Methods of peptide mapping and sequencing using MS are described in WO 95/252819, U.S. Pat. No. 5,538,897, U.S. Pat. No. 5,869,240, U.S. Pat. No. 5,572,259, and U.S. Pat. No. 5,696,376. See, also, Yates, J. Mass Spec., 33:1 (1998).

Data collected from a mass spectrometer typically comprises the intensity and mass to charge ratio for each detected event. Spectral data can be recorded in any suitable form, including, e.g., in graphical, numerical, or electronic formats, either in digital or analog form. Spectra are preferably recorded in a storage medium, including, e.g., magnetic, such as floppy disk, tape, or hard disk; optical, such as CD-ROM or laser-disc; or, ROM-CHIPS.

The mass spectrum of a given sample typically provides information on protein intensity, mass to charge ratio, and molecular weight. In preferred embodiments of the invention, the molecular weights of proteins in the sample are used as a matching criterion to query a database. The molecular weights are calculated conventionally, e.g., by subtracting the mass of the ionizing proton for singly-charged protonated molecular ions, by multiplying the measured mass/charge ratio by the number of charges for multiply-charged ions and subtracting the number of ionizing protons.

Various databases are useful in accordance with the present invention. Useful databases include, databases containing genomic sequences, expressed gene sequences, and/or expressed protein sequences. Preferred databases contain nucleotide sequence-derived molecular masses of proteins present in a known organism, organ, tissue, or cell-type. There are a number of algorithms to identify open reading frames (ORF) and convert nucleotide sequences into protein sequence and molecular weight information. Several publicly accessible databases are available, including, the SwissPROT/TrEMBL database (http://www.expasy.ch).

Typically, a mass spectrometer is equipped with commercial software that identifies peaks above a certain threshold level, calculates mass, charge, and intensity of detected ions. Correlating molecular weight with a given output peak can be accomplished directly from the spectral data, i.e., where the charge on an ion is one and the molecular weight is therefore equal to the numerator value minus the mass of the ionizing proton. However, protein ions can be complexed with various counter-ions and adducts, such as N, C, and K. In such a case, it would be expected that a given protein ion would exhibit multiple peaks, such as a triplet, representing different ionic states (or species) of the same protein. Thus, it may be necessary to analyze and process spectral data to determine families of

peaks arising from the same protein. This analysis can be carried out conventionally, e.g., as described by Mann et al., anal. Chem., 61:1702-1708 (1989).

In matching a molecular mass calculated from a mass spectrometer to a molecular mass predicted from a database, such as a genomic or expressed gene database, post-translation processing may have to be considered. There are various processing events which modify protein structure, including, proteolytic processing, removal of N-terminal methionine, acetylation, methylation, glycosylation, phosphorylation, etc.

A database can be queried for a range of proteins matching the molecular mass of the unknown. The range window can be determined by the accuracy of the instrument, the method by which the sample was prepared, etc. Based on the number of hits (where a hit is match) in the spectrum, the unknown protein or peptide is identified or classified.

Methods of identifying one or more HPP by mass spectrometry are useful for diagnosis and prognosis. Preferably, such methods are used to detect one or more HPP present in human plasma. Exemplary techniques are described in U.S. Patent Applications 02/0060290, 02/0137106, 02/0138208, 02/0142343, 02/0155509.

Diagnostic and Prognostic Uses

The nucleic acid molecules, proteins, protein homologues, and antibodies described herein can be used in one or more of the following methods: diagnostic assays, prognostic assays, monitoring clinical trials, and pharmacogenetics as further described herein.

The invention provides diagnostic and prognostic assays for detecting HPP nucleic acids and proteins, as further described. Also provided are diagnostic and prognostic assays for detecting interactions between HPPs and HPP target molecules, particularly natural agonists and antagonists.

The present invention provides methods for identifying polypeptides that are differentially expressed between two or more samples. "Differential expression" refers to differences in the quantity or quality of a polypeptide between samples. Such differences could result at any stage of protein expression from transcription through post-translational modification. For example, using protein array methods, two samples are bound to affinity spots on different sets of adsorbents (e.g., chips) and recognition maps are compared to identify polypeptides that are differentially retained by the two sets of adsorbents. Differential retention includes quantitative retention as well as qualitative differences in the polypeptide. For example, differences in post-translational modification of a protein can result in differences in recognition maps detectable as differences in binding characteristics (e.g., glycosylated proteins bind differently to lectin adsorbents) or differences in mass (e.g., post-

translational cleavage products). In certain embodiments, an adsorbent can have an array of affinity spots selected for a combination of markers diagnostic for a disease or syndrome.

Differences in polypeptide levels between samples (e.g., differentially expressed HPPs in plasma samples) can be identified by exposing the samples to a variety of conditions for analysis by desorption spectrometry (e.g., mass spectrometry). Proteins can be identified by detecting physicochemical characteristics (e.g., molecular mass), and this information can be used to search databases for proteins having similar profiles.

Preferred methods of detecting an HPP utilize mass spectrometry techniques. Such methods provide information about the size and character of the particular HPP isoform that is present in a sample, e.g., a biological sample submitted for diagnosis or prognosis. Mass spectrometry techniques are detailed in the section titled "Detection of HPPs by mass spectrometry". Example 1 outlines a preferred detection scheme, wherein a biological sample is separated by chromatography before characterization by mass spectrometry. The invention provides a method of detecting an HPP in a biological sample comprising the steps of: fractionating a biological sample (e.g., plasma, serum, lymph, cerebrospinal fluid, cell lysate of a particular tissue) by at least one chromatographic step; subjecting a fraction to mass spectrometry; and comparing the characteristics of polypeptide species observed in mass spectrometry with known characteristics of HPP polypeptides.

An especially preferred method includes detection of at least one HPP using retentate chromotography methods, including, for example, protein arrays or chips. Such methods are described in the section titled "Detection Using Protein Arrays." Preferably, said more than one HPP is detected in a biological sample, preferably plasma. A favored embodiment provides a protein chip capable of detecting an HPP on an addressable array representing proteins present in human plasma.

Accordingly one embodiment of the present invention involves a method of use (e.g., a diagnostic or prognostic assay) wherein a molecule of the present invention (e.g., an HPP, HPP nucleic acid, or antibody) is used to diagnose or prognose an HPP-related disorder or one in which any of the aforementioned HPP activities is indicated. In another embodiment, the present invention involves a method of use wherein a molecule of the present invention is used, for example, for the diagnosis or prognosis of subjects, preferably a human subject, in which any of the aforementioned activities is pathologically perturbed.

For example, the invention encompasses a method of determining whether an HPP is expressed within a biological sample comprising: a) contacting said biological sample with: i) a polynucleotide that hybridizes under stringent conditions to an HPP nucleic acid; or ii) a detectable polypeptide (e.g. antibody) that selectively binds to an HPP; and b) detecting the presence or absence

of hybridization between said polynucleotide and an RNA species within said sample, or the presence or absence of binding of said detectable polypeptide to a polypeptide within said sample. Detection of said hybridization or of said binding indicates that said HPP is expressed within said sample. Preferably, the polynucleotide is a primer, wherein said hybridization is detected by detecting the presence of an amplification product comprising said primer sequence, or the detectable polypeptide is an antibody.

In certain embodiments, detection involves the use of a probe/primer in a polymerase chain reaction (PCR) (see, e.g., U.S. Pat. Nos. 4,683,195 and 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (see, e.g., Landegren et al. (1988) Science 241:1077-1080; and Nakazawa et al. (1994) PNAS 91:360-364), the latter of which can be particularly useful for detecting point mutations in the HPP-encoding-gene (see Abravaya et al. (1995) Nucleic Acids Res. 23:675-682).

Also envisioned is a method of determining whether a mammal, preferably human, has an elevated or reduced level of expression of an HPP, comprising: a) providing a biological sample from said mammal; and b) comparing the amount of an HPP or of an HPP RNA species encoding an HPP within said biological sample with a level detected in a control sample. An increased amount of said HPP or said HPP RNA species within said biological sample compared to said level detected in or expected from said control sample indicates that said mammal has an elevated level of HPP expression, and a decreased amount of said HPP or said HPP RNA species within said biological sample compared to said level detected in or expected from said control sample indicates that said mammal has a reduced level of expression of an HPP.

The present invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, and monitoring clinical trials are used for prognostic purposes. Accordingly, one aspect of the present invention relates to diagnostic assays for determining HPP and/or nucleic acid expression as well as HPP activity, in the context of a biological sample (e.g., blood, plasma, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant HPP expression or activity. The invention also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a disorder associated with an HPP, nucleic acid expression or activity. For example, mutations in an HPP-encoding gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with HPP expression or activity.

The term "biological sample" is intended to include tissues, cells and biological fluids isolated from an individual, as well as tissues, cells and fluids present within an individual. That is, the detection methods of the invention can be used to detect an HPP mRNA, protein, or genomic DNA in a biological sample in vitro as well as in vivo. Prefered biological samples are biological fluids such as cell lysate, lymph, cerebrospinal fluid, blood, and especially blood plasma. For example, in vitro techniques for detection of an HPP mRNA include Northern hybridizations and in situ hybridizations. In vitro techniques for detection of an HPP include mass spectrometry, Enzyme Linked Immuno Sorbent Assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. In vitro techniques for detection of an HPP-encoding genomic DNA include Southern hybridizations. Furthermore, in vivo techniques for detection of an HPP include introducing into an individual a labeled anti- HPP antibody.

Pharmaceutical Compositions

One aspect of the invention relates to pharmaceutical compositions suitable for administration. In one embodiment the pharmaceutical composition comprises one or more HPP polypeptides, in conjunction with a pharmaceutically acceptable carrier. In another embodiment the pharmaceutical composition comprises compounds capable of detecting or modulating a HPP or a HPP biological activity including small molecules, peptides, HPP nucleic acid molecules, and anti-HPP antibodies of the invention. Such compositions typically comprise a pharmaceutically acceptable carrier. As used herein the language "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, e.g., intravenous, intradermal, subcutaneous, oral (e.g., inhalation), transdermal (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or

sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL® (BASF, Parsippany, N.J.) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as manitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Where the active compound is a protein, e.g., an anti-HPP antibody, sterile injectable solutions can be prepared by incorporating the active compound in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium and other required ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic

administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser which contains a suitable propellant, e.g., a gas such as carbon dioxide, or a nebulizer. Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art. Most preferably, active compound is delivered to a subject by intravenous injection.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Pat. No. 4,522,811, the disclosure of which is incorporated herein by reference in its entirety.

In a further embodiment, the active compound may be coated on a microchip drug delivery device. Such devices are useful for controlled delivery of proteinaceous compositions into the bloodstream, cerebrospinal fluid, lymph, or tissue of an individual without subjecting such compositions to digestion or subjecting the individual to injection. Methods of using microchip drug delivery devices are described in US Patents 6123861, 5797898 and US Patent application 20020119176A1, disclosures of which are hereby incorporated in their entireties.

It is especially advantageous to formulate oral or preferably parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of

the invention are dictated by and directly dependent on the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD50 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD50/ED50. Compounds which exhibit large therapeutic indices are preferred. While compounds that exhibit toxic side effects may be used, care should be taken to design a delivery system that targets such compounds to the site of affected tissue in order to minimize potential damage to uninfected cells and, thereby, reduce side effects.

The data obtained from the cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED50 with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For any compound used in the method of the invention, the therapeutically effective dose can be estimated initially from cell culture assays. A dose may be formulated in animal models to more accurately determine useful doses in humans. Levels in plasma may be measured, for example, by high performance liquid chromatography.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

Disease Therapies

The HPP polypeptides of the present invention as well as HPP modulators and HPP-related compositions of the invention can be used in the treatment or prevention of HPP-related disorders. Such diseases and disorders include, but are not limited to the diseases and disorders set forth below. Example 4 provides a method suitable for determining diseases and disorders in which HPP polypeptides of the present invention could be used as therapeutics, prognostics and/or diagnostics. However, it will be appreciated that there are other suitable methods known in the art, that can be used for this purpose.

Disease Therapies Related to Cell Proliferation and Cancer

In accordance with one aspect of the present invention, HPP-38 polypeptide is provided for the treatment of a cancer disease or a disease or condition associated with hyperplasia or for the prognosis or diagnosis of said diseases.

Polypeptide HPP-38 which had been detected in human plasma in accordance with the present invention, was found to have an amino acid sequence which is part of Esophageal cancer related gene 2 (ECRG2) Swiss-Prot P58062. In the context of the present invention the term HPP-38 polypeptide includes polypeptides of the sequence as set forth in SEQ ID No: 391 and 392. Also encompassed are variants and derivatives wherein the variants and derivatives have a sequence identical to the sequences forth in SEQ ID No: 391 and 392 of desirably at least 80%, more desirably at least 85%, preferably at least 90%, more preferably at least 95%, still more preferably at least 99%. The variants and derivatives may have one, two or three amino acid substitutions, deletions or insertions relative to an amino acid sequence set forth in SEQ ID No: 391 and 392. The variants and derivatives may also be chemically modified as described herein. HPP-38 polypeptide was synthezised by GeneProt, Inc (Geneva, Switzerland) and, in an approach as described in Example 4, the peptide was injected into mice and gene expression profiling on many organs performed. Table 4 shows that HPP-38 polypeptide affects expression of genes which are involved in the positive regulation of apoptosis, genes with indication in breast cancer, stress response genes and tumor suppressor genes. In addition, many RNAs encoding tight junction proteins were downregulated in a concerted manner in blood, heart, kidney, liver and spleen. All of those gene groups can be linked to regulation of cell growth. To confirm our finding ECRG2 was tested for its growth regulatory activity in a cell growth assay at MDS Pharma Services. ECRG2 was added to the supernatant of 15 cancer cell lines at concentrations ranging from 0.01 to 100 micromolar and cell growth was measured over time. ECRG2 was able to significantly inhibit the growth (< 50% of cell proliferation) of 11 of the 15 cell lines tested, including MCF-7 (breast), DLD-1 (colon), A-498 (kidney), HepG2 (Liver), A549 (lung), SK-MEL-5 (melanoma), SK-N-MC (neuroepithelioma), PANC-1 (pancreas), PC-3 (prostate), A431 (skin), MES-SA (uterus). IC-50 was below 20 micromolar for the neuroepithelioma, prostate, skin, and uterus cell lines.

Accordingly, the present invention now provides HPP-38 polypeptide as suitable therapeutic for the treatment of a cancer disease or a disease or condition associated with hyperplasia comprising administering an effective amount of an HPP-38 polypeptide to a mammal, including a human, suffering from said disease. Preferably, the cancer disease is selected from the group consisting of neuroepithelioma, prostate cancer, basal cell carcinoma, squamous cell carcinoma, melanomas, and cervical intraepithelial neoplasia. In another preferred emobiment, the disease or condition associated

with hyperplasia is a disease or condition selected from the group consisting of fibrosis, prostatic hyperplasia, adrenal hyperplasia, endometrial hyperplasia, psoriasis, hyperplasia due to inflammation. In one preferred embodiment the use of HPP-38 polypeptide in medicine is provided.

According to another aspect, the present invention provides a method for the prognosis or diagnosis of a cancer disease or a disease or condition associated with hyperplasia comprising detecting the plasma level of a HPP-38 polypeptide, wherein an increased level is indicative of a cancer disease or a disease or condition associated with hyperplasia. An increased HPP-38 polypeptide plasma level within the context of the present invention is relative to the HPP-38 polypeptide plasma level as found in individuals which do not suffer of a cancer disease or a disease or condition associated with hyperplasia. The increase is preferably at least 1.2 fold, more preferably at least 1.5 fold, 2 fold, 3 fold, 5 fold or 10 fold.

According to another aspect, the present invention provides a method for the prognosis or diagnosis of a cancer disease or a disease or condition associated with hyperplasia comprising i) detecting a level of expression of at least one gene identified in Table 4 in a sample of a suitable tissue obtained from the subject to provide a first value; and ii) comparing the first value with a level of expression of said gene from a disease-free subject, wherein a greater or smaller expression level in the subject sample as compared to the sample from the disease-free subject is indicative of the subject being predisposed to or having a cancer disease or a disease or condition associated with hyperplasia. Gene expression may be detected on mRNA or protein level. Suitable tissues include, but are not limited to skin, prostate, pancreas, uterus, lung, liver, intestines, kidney. The mRNA expression level may be detected by any suitable technique, such as for instance Microarray analysis, Northern blot analysis, reverse transcription PCR and real time quantitative PCR. Likewise, the protein level may be detected by any suitable technique, such as for instance through western blotting by utilizing a labeled probe specific for the protein.

In a preferred embodiment of the above aspects, the gene(s) are selected from the gene(s) set forth in Table 4 which are upregulated or downregulated. Preferably, the gene(s) are selected from the gene(s) set forth in Table 4 which are upregulated 1.2 fold or more, 1.3 fold or more, or 1.5 fold or more; or from the gene(s) selected from the genes set forth in Table 4 are downregulated 0.8 fold or less, 0.7 fold or less. In yet another preferred embodiment of the above aspects, the expression of at least 1, 2, 3, 4 or 5 genes is measured.

According to another aspect, the present invention provides a method of identifying a modulator of a cancer disease or a disease or condition associated with hyperplasia comprising i) contacting a test compound with a HPP-38 polypeptide under sample conditions permissive for HPP-

38 biological activity; ii) determining the level of said at least one HPP-38 biological activity; iii) comparing said level to that of a control sample lacking said test compound. In a preferred embodiment said test compound, which causes said level to change, is selected for further testing as a HPP-38 modulator for the prophylactic and/or therapeutic treatment of a cancer disease or a disease or condition associated with hyperplasia. In a preferred embodiment, the level of HPP-38 biological activity is measured by detecting the level of expression of one or more genes set forth in Table 4.

Disease Therapies Related to Defects in Iron Transport or Iron Balance

Polypeptides HPP-13, which had been detected in human plasma in accordance with the present invention, was found to have an amino acid sequence which is part of human thymosin beta 4 (Swiss-Prot P01253). In the context of the present invention the term HPP-13 polypeptides includes polypeptides of the sequence as set forth in SEQ ID No: 393 (human form and short mouse isoform) and SEQ ID No: 394 (long mouse isoform). Also encompassed are variants and derivatives wherein the variants and derivatives have a sequence identical to the sequences forth in SEQ ID No: 393 and 394 of desirably at least 80%, more desirably at least 85%, preferably at least 90%, more preferably at least 95%, still more preferably at least 99%. The variants and derivatives may have one, two or three amino acid substitutions, deletions or insertions relative to an amino acid sequence set forth in SEQ ID No: 393 and 394. The variants and derivatives may also be chemically modified as described herein. HPP-13 polypeptides were synthezised by GeneProt, Inc (Geneva, Switzerland) and, in an approach as described in Example 4, the peptides were injected into mice and gene expression profiling on many organs performed. Table 6, 7, 8, 9 and/or 10 shows that HPP-13 polypeptides affect expression of genes which are involved in heme biosynthesis and metabolism, porphyrin biosynthesis and metabolism and erythropoiesis. Additionally, genes involved in dietary iron balance, iron transport are also differentially regulated.

Accordingly, the present invention now provides HPP-13 polypeptides for the treatment of conditions related to diseases or conditions where body iron balance is altered, leading to iron overload diseases, anemia or deficient red blood cell production. In one embodiment, HPP-13 polypeptides are provided as suitable therapeutics for the treatment of a disease or condition associated with iron balance or iron transport comprising administering an effective amount of an HPP-13 polypeptide to a mammal, including a human, suffering from said disease. Preferably, the disease or condition associated with iron balance or iron transport is selected from the group consisting of hemochromatosis, hereditary hemochromatosis, juvenile hemochromatosis, thalassemia,

conditions related to iron-overload, anemia, sickle cell anemia. In one preferred embodiment the use of HPP-13 polypeptides in medicine is provided.

According to another aspect, the present invention provides a method for the prognosis or diagnosis of a disease or condition associated with iron balance or iron transport comprising detecting the plasma level of an HPP-13 polypeptide, wherein an increased level is indicative of a disease or condition associated with iron balance or iron transport. An increased HPP-13 polypeptides plasma level within the context of the present invention is relative to the HPP-13 polypeptide plasma level as found in individuals which do not suffer of a disease or condition associated with iron balance or iron transport. The increase is preferably at least 1.2 fold, more preferably at least 1.5 fold, 2 fold, 3 fold, 5 fold or 10 fold.

According to another aspect, the present invention provides a method for the prognosis or diagnosis of a disease or condition associated with iron balance or iron transport comprising i) detecting a level of expression of at least one gene identified in Table 6, 7, 8, 9 and/or 10 in a sample of a suitable tissue obtained from the subject to provide a first value; and ii) comparing the first value with a level of expression of said gene from a disease-free subject, wherein a greater or smaller expression level in the subject sample as compared to the sample from the disease-free subject is indicative of the subject being predisposed to or having a disease or condition associated with iron balance or iron transport. Gene expression may be detected on mRNA or protein level. Suitable tissues include, but are not limited to liver, heart, intestines such as duodenum, spleen, bone marrow. The mRNA expression level may be detected by any suitable technique, such as for instance Microarray analysis, Northern blot analysis, reverse transcription PCR and real time quantitative PCR. Likewise, the protein level may be detected by any suitable technique, such as for instance through western blotting by utilizing a labeled probe specific for the protein.

In a preferred embodiment of the above aspects, the gene(s) are selected from the gene(s) set forth in Table 6, 7, 8, 9 and/or 10 which are upregulated or downregulated. Preferably, the gene(s) are selected from the gene(s) set forth in Table 6, 7, 8, 9 and/or 10 which are upregulated 1.2 fold or more, 1.3 fold or more, or 1.5 fold or more; or from the gene(s) selected from the genes set forth in Table 6, 7, 8, 9 and/or 10 are downregulated 0.8 fold or less, 0.7 fold or less, or 0.6 fold or less. In yet another preferred embodiment of the above aspects, the expression of at least 1, 2, 3, 4 or 5 genes is measured.

According to another aspect, the present invention provides a method of identifying a modulator of a disease or condition associated with iron balance or iron transport comprising i) contacting a test compound with a HPP-13 polypeptide under sample conditions permissive for HPP-

13 biological activity; ii) determining the level of said at least one HPP-13 biological activity; iii) comparing said level to that of a control sample lacking said test compound. In a preferred embodiment said test compound, which causes said level to change, is selected for further testing as a HPP-13 modulator for the prophylactic and/or therapeutic treatment of a disease or condition associated with iron balance or iron transport. In a preferred embodiment, the level of HPP-13 biological activity is measured by detecting the level of expression of one or more genes set forth in Table 6, 7, 8, 9 and/or 10.

Disease Therapies Related to Neurodegeneration

Table 11 shows that treatment of mice with HPP-13 polypeptide resulted in gene expression profiles showing that these polypeptides would be useful in the treatment of conditions of neurodegeneration and peripheral neuropathies, such as multiple sclerosis, demyelinating diseases, Guillian-Barré disease, diabetic neuropathy, chemotherapy induced neuropathy, autoimmune related neuropathy, CNS-related neuropathies, such as Alzheimer's disease and neuronal injury related for example to stoke (nervous system ischemia).

In addition GPA101 polypeptide is provided in accordance with the present invention to be useful for the treatment of the above conditions. GAP101 is a polypeptide with a randomized sequence of HPP-13. In the context of the present invention the term GPA101 polypeptide includes polypeptides of the sequence as set forth in SEQ ID No: 397 as well as variants and derivatives as described above. Thus, in one embodiment the present invention provides a polypeptide comprising the amino acid sequence set forth in SEQ ID No: 397, in a preferred embodiment, the present invention provides a polypeptide consisting of the sequence set forth in SEQ ID No: 397.

Accordingly, the present invention now provides HPP-13 and GPA101 polypeptides as suitable therapeutics for the treatment of a disease or condition associated with neurodegeneration comprising administering an effective amount of an HPP-13 or GPA101 polypeptides to a mammal, including a human, suffering from said disease. Preferably, the disease or condition associated with neurodegeneration is selected from the group consisting of spinal cord injuries or CNS injuries, , Alzheimer's, Parkinson's, multiple sclerosis, , ALS (amyotrophic lateral sclerosis), peripheral neuropathy, Guillian-Barré disease, diabetic neuropathy, demyelinating neuropathies. In one preferred embodiment the use of HPP-13 or GPA101 polypeptide in medicine is provided.

According to another aspect, the present invention provides a method for the prognosis or diagnosis of a disease or condition associated with neurodegeneration comprising detecting the plasma level of a HPP-13 polypeptide, wherein an increased level is indicative of a disease or condition associated with

neurodegeneration. An increased HPP-13 polypeptide plasma level within the context of the present invention is relative to the HPP-13 polypeptide plasma level as found in individuals which do not suffer of a disease or condition associated with neurodegeneration. The increase is preferably at least 1.2 fold, more preferably at least 1.5 fold, 2 fold, 3 fold, 5 fold or 10 fold.

According to another aspect, the present invention provides a method for the prognosis or diagnosis of a disease or condition associated with neurodegeneration comprising i) detecting a level of expression of at least one gene identified in Table 11 in a sample of a suitable tissue obtained from the subject to provide a first value; and ii) comparing the first value with a level of expression of said gene from a disease-free subject, wherein a greater or smaller expression level in the subject sample as compared to the sample from the disease-free subject is indicative of the subject being predisposed to or having a disease or condition associated with neurodegeneration. Gene expression may be detected on mRNA or protein level. Suitable tissues include, but are not limited to brain, spinal cord, neuromotor tissue, peripheral nerves, central and peripheral nervous tissues. The mRNA expression level may be detected by any suitable technique, such as for instance Microarray analysis, Northern blot analysis, reverse transcription PCR and real time quantitative PCR. Likewise, the protein level may be detected by any suitable technique, such as for instance through western blotting by utilizing a labeled probe specific for the protein.

In a preferred embodiment of the above aspects, the gene(s) are selected from the gene(s) set forth in Table 11 which are upregulated or downregulated. Preferably, the gene(s) are selected from the gene(s) set forth in Table 11 which are upregulated 1.2 fold or more, 1.3 fold or more, or 1.5 fold or more; or from the gene(s) selected from the genes set forth in Table 11 are downregulated 0.8 fold or less, 0.7 fold or less, or 0.6 fold or less. In yet another preferred embodiment of the above aspects, the expression of at least 1, 2, 3, 4 or 5 genes is measured.

According to another aspect, the present invention provides a method of identifying a modulator of a disease or condition associated with neurodegeneration comprising i) contacting a test compound with a HPP-13 or GPA101 polypeptide under sample conditions permissive for HPP-13 or GPA101 biological activity; ii) determining the level of said at least one HPP-13 or GPA101 biological activity; iii) comparing said level to that of a control sample lacking said test compound. In a preferred embodiment said test compound, which causes said level to change, is selected for further testing as a HPP-13 or GPA101 modulator for the prophylactic and/or therapeutic treatment of a disease or condition associated with neurodegeneration. In a preferred embodiment, the level of HPP-13 biological activity is measured and the expression of one or more genes set forth in Table 11 is detected.

Disease Therapies Related to Defects in Glucose Metabolism

Polypeptide HPP-23 which had been detected in human plasma in accordance with the present invention, was found to have an amino acid sequence which is part of Pancreastatin (Swiss-Prot P10645). In the context of the present invention the term HPP-23 polypeptide includes polypeptides of the sequence as set forth in SEQ ID No: 395 and SEQ ID No: 396. In a particularly preferred embodiment the polypeptide is not amidated. Also encompassed are variants and derivatives wherein the variants and derivatives have a sequence identical to the sequences forth in SEQ ID No: 395 and SEQ ID No: 396 of desirably at least 80%, more desirably at least 85%, preferably at least 90%, more preferably at least 95%, still more preferably at least 99%. The variants and derivatives may have one, two or three amino acid substitutions, deletions or insertions relative to an amino acid sequence set forth in SEQ ID No: 395 and SEQ ID No: 396. The variants and derivatives may also be chemically modified as described herein. HPP-23 polypeptide was synthezised by GeneProt, Inc (Geneva, Switzerland) and, in an approach as described in Example 4, the peptide was injected into mice and gene expression profiling on many organs performed. In the brain and other organs, HPP-23 polypeptide injection revealed a strong effect the RNA expression levels of genes involved in glucose metabolism, other carbohydrate catabolism pathways, vasculogenesis and inflammatory responses (Table 12). In addition the major steps of the signalling pathway of pancreastatin could be reconstituted.

HPP-23 was tested for its modulatory effect on glucose levels in three mouse models at MDS Pharma Services: fasted ICR mice, glucose-loaded ICR mice, and db/db (NIDDM, non-insulin dependent diabetic mellitus)-mice, which are a model of type 2 diabetes. At a dose of 10mg/kg, non-amidated pancreastatin significantly reduced serum glucose levels in glucose-loaded mice by 20% compared to vehicle. This is the first record of a biological activity of a non-amidated form of pancreastatin. The biological activity is regulation of serum glucose levels.

Accordingly, the present invention now provides HPP-23 polypeptide as suitable therapeutic for the treatment of a diseases with dysregulated serum glucose comprising administering an effective amount of an HPP-23 polypeptide to a mammal, including a human, suffering from said disease. Preferably, the diseases with dysregulated serum glucose is diabetes or other hyperglycemic conditions. In a particularly preferred embodiment, HPP-23 reduces blood glucose levels when administered to a mammal, including a human. In one preferred embodiment the use of HPP-23 in medicine is provided.

According to another aspect, the present invention provides a method for the prognosis or diagnosis of

a diseases with dysregulated serum glucose comprising detecting the plasma level of a HPP-23 polypeptide, wherein an increased level is indicative of a disease with dysregulated serum glucose. An increased HPP-23 polypeptide plasma level within the context of the present invention is relative to the HPP-23 polypeptide plasma level as found in individuals which do not suffer of a disease with dysregulated serum glucose. The increase is preferably at least 1.2 fold, more preferably at least 1.5 fold, 2 fold, 3 fold, 5 fold or 10 fold.

According to another aspect, the present invention provides a method for the prognosis or diagnosis of a disease with dysregulated serum glucose comprising i) detecting a level of expression of at least one gene identified in Table 12 in a sample of a suitable tissue obtained from the subject to provide a first value; and ii) comparing the first value with a level of expression of said gene from a disease-free subject, wherein a greater or smaller expression level in the subject sample as compared to the sample from the disease-free subject is indicative of the subject being predisposed to or having a disease with dysregulated serum glucose. Gene expression may be detected on mRNA or protein level. Suitable tissues include, but are not limited to adipose (fat) tissue, heart, pancreas, muscle, brain. The mRNA expression level may be detected by any suitable technique, such as for instance Microarray analysis, Northern blot analysis, reverse transcription PCR and real time quantitative PCR. Likewise, the protein level may be detected by any suitable technique, such as for instance through western blotting by utilizing a labeled probe specific for the protein.

In a preferred embodiment of the above aspects, the gene(s) are selected from the gene(s) set forth in Table 12 which are upregulated or downregulated. Preferably, the gene(s) are selected from the gene(s) set forth in Table 12 which are upregulated 1.2 fold or more, 1.3 fold or more, or 1.5 fold or more; or from the gene(s) selected from the genes set forth in Table 12 are downregulated 0.8 fold or less, 0.7 fold or less, or 0.6 fold or less. In yet another preferred embodiment of the above aspects, the expression of at least 1, 2, 3, 4 or 5 genes is measured.

According to another aspect, the present invention provides a method of identifying a modulator of a disease with dysregulated serum glucose comprising i) contacting a test compound with a HPP-23 polypeptide under sample conditions permissive for HPP-23 biological activity; ii) determining the level of said at least one HPP-23 biological activity; iii) comparing said level to that of a control sample lacking said test compound. In a preferred embodiment said test compound, which causes said level to change, is selected for further testing as a HPP-23 modulator for the prophylactic and/or therapeutic treatment of a disease with dysregulated serum glucose. In a preferred embodiment, the level of HPP-23 biological activity is measured by detecting the level of expression of one or more genes set forth in Table 12.

Disease Therapies Related to Metabolic Disorders

In a further aspect of the present invention, HPP-23 polypeptide is provided as suitable therapeutic for the treatment of a metabolic disorder, in particular of amyloidosis. Also provided as part of the invention is HPP-23 polypeptide as suitable treatment for arrhythmia, in particular bradycardia, tachycardia, sick sinus syndrome, and angiogenesis, in particular, stroke, macular regeneration, cancer.

Amyloidosis is a group of incompletely understood metabolic disorders resulting from the deposition of protein-containing fibrils (amyloid) in tissues. The disease may cause localized or widespread organ failure. Amyloid may infiltrate many organs, including heart and blood vessels, brain and peripheral nerves. Hence, the clinical manifestations of amyloidosis are enormously varied, and the disease may mimic other conditions ranging from nephritic syndrome to dementias or congestive heart failure. Pathways of oxidative stress seem to be causative for the development of amyloid fibrils. Oxidative stress precipitates both nuclear DNA degradation and membrane phosphatidylserine exposure in neuronal and vascular cells to promote loss of cellular integrity, microglial phagocytosis, and thrombotic destruction. Critical in the ability to foster cell survival during oxidative stress is the modulation of the metabotropic glutamate system, cell cycle regulation in post-mitotic neurons, and control of GSK-3beta activity and presenilin integrity. These cellular pathways ultimately converge upon more central cellular mechanisms that involve maintenance of mitochondrial membrane permeability through Bcl-2 family members, trophic factors, and mitochondrial energy reserves.

Pancreastatin in brain tissue: In brain of HPP-23 polypeptide treated mice it has been found in accordance with the present invention that amyloidosis-diseases are affected by HPP-23 polypeptide. HPP-23 polypeptide upregulates presenilin1, a large panel of peroxiredoxin genes, mitochondrial NADH-dehydrogenases, endothelial nitric oxide, cytochrome c-oxidases (15 probe sets). (All those groups were not affected by a control). Those genes indicate big changes in the redox-system and point at oxidative stress. In addition the expression of many cell cycle genes (cyclins and cyclin-dependent kinases) are changed.

Another indicator of an involvement of Pancreastatin and HPP-23 polypeptide in the development of amyloidosis is a strong upregulation of tubulin genes (tubulin alpha1,2,4,beta,gamma, cofactor alpha). Tubulin-amyloid depsositions are found in familial cerebral amyloid angiopathy (Baumann et al., Biochem Biophys Res Comm, 1996, 219: 238-242). (Again, those changes are not found in control brains).

Strong expression of presenilin, which is involved in Notch- as well as amyloid precursor protein (APP) processing, and of apolipoprotein E (apoE) have been shown to be part of a mechanism for the progression of familial Alzheimer's disease (Tezapsidis et al, FASEB 2003, 17:1322-1324). Both presenilin and apoE were upregulated by HPP-23 polypeptide. Amyloid precursor genes (APP) and various APP-binding proteins are also upregulated by HPP-23 polypeptide. Schipper (Ann N Y Acad Sci 2004,1012:84-93) describes that heme oxygenase (HO-1) expression is stimulated under pro-oxidant stimuli such as dopamine, hydrogen peroxide, beta-amyloid and others, and that HO-1 is found upregulated in CNS tissues affected by Alzheimer's disease, Parkinson's disease, multiple sclerosis and other degenerative and non-degenerative CNS diseases. HPP-23 polypeptide leads to an upregulation of HO-1 in brain.

Ferreiro et al (J Neurosci Res, 2004,76:872-880) published that in-vitro cultured neurons treated with amyloid-beta peptides demonstrated neuronal loss by apoptosis, which at least in part was due to the perturbation of intracellular Ca(2+) homeostasis. Inhibition of Ca(2+)-release from the endoplasmic reticulum, mediated by the ryanodine receptor (Ryr) and IP(3)R abrogated this neurotoxic effect. Ryr is about two-fold downregulated in HPP-23 polypeptide treated brain.

Pancreastatin in heart tissue: Ryanodine receptor per se is not affected in the hearts of pancreastatin treated animals, However, many ryr binding proteins are downregulated, such as FKBP12, calmodulin, sorcin, triadin, and phosphatase 1. Sorcin binds to presenilin1, which is also downregulated in heart. Presenilin is part of the Notch pathway, consisting, among others, of ADAM17, notch, and the targets snail,hes1, and the homeobox gene msx. While snail and hes1 were upregulated, all other members were downregulated. An inhibitor of notch, numb, was upregulated, pointing at a common inhibition of the pathway. Another presenilin binding protein is restin. Disruption of this complex is associated with both decreased secretion of endogenous amyloid beta peptide and decreased uptake of exogenous amyloid beta from the medium of cultured cells (Tezapsidis et al, FASEB 2003,17:1322-1324). Restin was found upregulated in the heart of HPP-23 polypeptide treated mice.

The Notch signalling pathway is essential in cardiac development (e.g. Timmerman et al, Genes Dev 2004 18:99-115). Furthermore it is crosstalking with VEGF (vascular endothelial growth factor), e.g. notch 4 is an inhibitor of VEGF signaling, while VEGF and notch 1 regulate sprouting (Liu et al. Mol Cell Biol 2003,23:14-25). In addition to changes in VEGF expression both in heart and brain, we detect changes in angiomotin and angiopoietin as well as other angiogenesis-related genes. Nakajima et al published (Mech dev 2003,120:657-667) that mice lacking presenilin-1 develop abnormal blood vessels. In the eye of our data this may be due the participation of presenilin in the

notch pathway.

Taken together, these gene expression changes in the heart indicate a participation of HPP-23 polypeptide in conditions such as arrhythmia (bradycardia, tachycardia, sick sinus syndrome), and angiogenesis (e.g. stroke, macular regeneration, cancer). Accordingly, the present invention provides HPP-23 polypeptides for therapeutic, prognostic and diagnostic methods as well as for screening methods (e.g. method for identifying modulators) as described above for these indications.

Disclosures of the references cited throughout the specification are incorporated by reference in their entireties. Having generally described this invention, a further understanding can be obtained by reference to certain specific examples provided herein for purposes of illustration only, and are not intended to be limiting unless otherwise specified.

EXAMPLES

Example 1: Characterization of HPP levels

Portions of plasma from more than 50 healthy male volunteers were pooled in order to dilute phenotypic differences and to provide a large pool volume. Blood (100-450 ml) was obtained using standard veinous puncture procedures in a medical centre setting after informed written consent. Samples were barcoded and plasma was prepared by centrifugation and removal of white cells on filters by standard techniques. Times, temperatures and centrifugation conditions and subsequent procedures were rigorously controlled to ensure similar treatment of all samples. Protease inhibitor (Complete, Roche) was added according to the manufacturer's instructions and mixed gently to ensure dissolution. Plasma samples were then frozen and stored at -80°C. After careful consideration of medical history and clinical chemistry parameters, portions of at least 50 samples were pooled. A volume of 2.5L (of the 6 L total) was subjected to separation by multiple chromatography steps according to the Microprot.TM process as follows:

Step 1: HSA/IgG depletion

125 ml frozen plasma were defrost and filtered on 0.45 µm sterile filter in a sterile hood.

Filtrate was injected on two inline columns of respectively 300 ml of HSA ligand Sepharose fast Flow column (Amersham, Upsala, Sweden), 5cm ID, 15 cm length; and 100 ml Protein G Sepharose fast Flow column (Amersham, Upsala, Sweden), 5 cm ID, 5 cm length.

Columns were equilibrated and washed with 50 mM PO4 buffer, pH 7.1, 0.15M NaCl. Flow

rate was 5 ml/min.

Non-retained fraction (53g of depleted polypeptides) was frozen until second step. Twenty runs were performed.

Step 2: Gel Filtration / Reverse Phase Capture step

Sample from step 1 was defrosted and filtered on 0.45 µm sterile filter in a sterile hood.

Filtrate was injected on two in line gel filtration columns: 2 X 9.5 litres Superdex 75 (Amersham, UK) column, 14 cm ID, 62 cm length. Column was equilibrated with 50mM PO4 buffer pH 7.4, 0.1 M NaCl, 8M urea. Hydrophobic impurities were retained on a reverse phase precolumn: 150 ml PLRPS (Polymer Labs, UK). Precolumn was switched for sample injection. Gel filtration was performed at a flow rate of 40 ml/min.

Low molecular weight proteins (<20 kDa) were oriented to in line reverse phase capture column: 50 ml PLRPS 100 angstroms (Polymer labs, UK). The three-way valve controlling injection on PLRPS column was switched at a cut-off of 33 mAU (280 nm) to send gel filtration eluate into reverse phase capture column. This cut-off value was established by first using SDS-PAGE to provide an estimated range of OD values and by subsequently evaluating three cut-off values (high, median and low values of OD range). The final cut-off value was chosen to maximize the low molecular weight protein obtained, with a low molecular protein proportion of at least 85%. Low molecular weight proteins and peptides were eluted from reverse phase capture PLRPS column by one column volume gradient of 0.1% TFA, 80% CH3CN in water.

Approximately 1.5 g of small proteins, of which 1.3 g was <20 kDa, were yielded as determined by analytical gel filtration HPLC monitored at 210 nm with a BSA standard. Eluate fractions (50 ml) were frozen until next step. Twenty runs were performed. At the end of this step, all reverse phase eluates were defrosted, pooled (1 liter) and shared in 7 polypropylene containers (143 ml). Containers were kept at –20°C until use for next step.

Step 3: Cation Exchange

Sample from step 2 (147 ml) was defrosted and mixed with an equal volume of cation exchange buffer A (Gly/HCl buffer 50 mM, pH 2.7, urea 8M).

Sample was injected on a 100 ml Source 15S column (Amersham, Upsala, Sweden), 35 mm ID, 100 mm length. Column was equilibrated and washed with buffer A. Flow rate was 10 ml/min.

Proteins and peptides were eluted with step gradient from 100% buffer A until 100 % buffer

B (buffer A containing 1M NaCl):

3 column volumes 7.5% B (75 mM NaCl)
3 column volumes 10% B (100 mM NaCl)
3 column volumes 17.5% B (175 mM NaCl)
2 column volumes 22.5% B (225 mM NaCl)
2 column volumes 27.5% B (275 mM NaCl)
2 column volumes 100% B (1 M NaCl)

45 to 60 fractions were collected based on peak. Seven runs were conducted. After 7 runs were achieved, fractions were pooled intra and inter run in order to obtain 18 fractions. Fractions were kept at –20°C until use for next step.

Step 4: Reduction/Alkylation and Reverse Phase HPLC Fractionation 1

After adjusting the pH to 8.5 with concentrated Tris-HCl, each of the 18 cation exchange fractions was reduced with dithioerythritol (DTE, 30 mM, 3 hours at 37°C) and alkylated with iodoacetamide (120 mM, 1 hour 25°C in the dark). The latter reaction was stopped with the addition of DTE (30 mM) followed by acidification (TFA, 0.1 %). The fractions were then injected on an Uptispher C8, 5 um, 300 angstroms column (Interchim, France), 21 mm ID, 150 mm length. Injection was performed with a 10 ml/min flow rate.

C8 column was equilibrated and washed with 0.1 % TFA in water (solution A). Proteins and peptides were eluted with a biphasic gradient from 100% A until 100% B (0.1% TFA, 80% CH3CN in water) in 60 min. Flow rate was 20 ml/min. Thirty fractions of 40 ml were collected.

Based on the measured optical density (OD) at 280 nm of each fraction, which reflects the protein concentration in that fraction, aliquots of similar protein content were created for each fraction.

All aliquots were frozen and kept for further use except one per fraction which was dried with a Speed Vac (Savant, Fischer, Geneva) after addition of 500 ul 10% glycerol in water in each fraction, in order to prevent excess drying. Dried fractions were kept at -20°C until use for next step.

Step 5: Reverse Phase HPLC Fractionation 2

Dried samples from step 4 were resuspended in 1 ml of solution A (0.03% TFA in water) and injected on a Vydac LCMS C4 column, 5 micrometers, 300 angstroms (Vydac, USA), 4.6 mm ID, 150

mm length. Flow rate was 0.8 ml/min.

C4 column was equilibrated and washed with solution A and proteins and peptides were eluted with a biphasic gradient adapted to elution position of the sample in Reverse Phase HPLC Fractionation 1. Intact mass data were acquired using Electrospray Ion Trap Mass spectrometry. Sixteen different gradients were used with a CH3CN concentration range minus and plus 5% CH3CN of RP1 fraction corresponding solvent concentration. For proteins eluted in RP1 with a solvent concentration equal to or greater than 30 % CH3CN, the starting elution conditions for the RP2 gradient was set, in CH3CN percentage, at the RP1 elution concentration minus 30%. Twenty-four eluted fractions were collected in a deep well plate, adopting optimized different collection configurations designed for optimal SpeedVac concentration and further robotic treatment.

Step 6: Mass detection

12,960 (18 x 30 x 24) fractions were collected following reverse phase HPLC fractionation 2 into 96-well deep well plates (DWP). A small proportion (2.5%) of the volume was diverted to online analysis using LC-ESI-MS (Bruker Esquire). Aliquots of undigested proteins were mixed with MALDI matrices, and spotted on MALDI plates together with mass calibration standards and sensitivity standards. Automated spotting devices (Bruker MALDI sample prep. Robots) were used. Two different MALDI matrices were employed: sinapic acid (SA), also known as sinapinic acid, trans-3,5-dimethoxy-4-hydroxycinnamic acid, and alpha-cyano-4-hydroxycinnamic acid (HCCA). MALDI plates were subjected to mass detection using Bruker Reflex III MALDI MS apparati. The 96-well plates were stored at +4 C.

96-well plates (DWP) were recovered and subjected to two sequential concentration steps. Volumes were concentrated from 0.8 ml to about 50 microl per well by drying with a SpeedVac, and then resolubilized to *ca.* 200 microl and reconcentrated to about 50 microl per well, and stored at +4 C. Proteins were then digested by re-buffering, adding trypsin to the wells, sealing and incubating the plates at 37 C for 12 hours, followed by quenching (addition of formic acid to bring the pH down to 2.0). The concentration of trypsin to be added to the wells was adjusted based on the OD at 280 nm recorded for each particular fraction. This ensured an optimal use of trypsin and a complete digestion of the most concentrated fractions. Automated spotting devices (Bruker MALDI sample prep. Robots) were used to deposit a volume from each well, pre-mixed with a HCCA matrix onto a MALDI plate together with sensitivity and mass calibration standards. MALDI plates were analyzed using a Bruker Reflex III MALDI MS device. Contents from each well of the 96 well plates were analyzed with LC-ESI-MS-MS Bruker Esquire ESI Ion-Trap MS devices.

Step 7: Detection and Identification of Low Abundance Peptides in Human Plasma

Separated fractions are further subjected to mass spectrometry (both MALDI and LC-ESI-MS-MS) for separation and detection.

More than 1.5 million MS/MS spectra were generated and 330 000 used for manual testing and validation of the algorithms developed for automated identifications. Intact mass data, Peptide Mass Fingerprints and peptide sequence data were integrated for protein identification and characterization. Proteins were identified using Mascot software (Matrix Science Ltd., London, UK), and results from peptide identification were checked by manual analysis of the spectra. MS/MS spectra were interpreted with a custom identification engine (Olav) which accessed a set of 6 different databases (SwissProt, public EST and Genomic sequence data, and Patent databases). An integration step confirmed the consistency of the global identification across the different databases. Annotation (automatic and manual) was performed on the validated identifications to further characterize important features of the observed polypeptides.

The methods of protein separation and identification according to the invention are extremely sensitive. The Microprot.TM process is able to detect very low abundance proteins with a plasma concentration in the range of 50 pM. The accuracy was confirmed while carrying out the presently described methods. In particular, proteins with a well-characterized role in human plasma were detected.

Example 2: Chemical Synthesis of HPPs

In this example, an HPP of the invention is synthesized. Peptide fragment intermediates are first synthesized and then assembled into the desired polypeptide.

An HPP can initially be prepared in, e.g. 5 fragments, selected to have a Cys residue at the N-terminus of the fragment to be coupled. Fragment 1 is initially coupled to fragment 2 to give a first product, then after preparative HPLC purification, the first product is coupled to fragment 3 to give a second product. After preparative HPLC purification, the second product is coupled to fragment 4 to give a third product. Finally, after preparative HPLC purification, the third product is coupled to fragment 5 to give the desired polypeptide, which is purified and refolded.

Thioester formation

Fragments 2, 3, 4, and 5 are synthesized on a thioester generating resin, as described above. For this purpose the following resin is prepared: S-acetylthioglycolic acid pentafluorophenylester is coupled to a Leu-PAM resin under conditions essentially as described by Hackeng et al (1999). In the first

case, the resulting resin is used as a starting resin for peptide chain elongation on a 0.2 mmol scale after removal of the acetyl protecting group with a 30 min treatment with 10% mercaptoethanol, 10% piperidine in DMF. The N^{α} of the N-terminal Cys residues of fragments 2 through 5 are protected by coupling a Boc-thioproline (Boc-SPr, i.e. Boc-L-thioproline) to the terminus of the respective chains instead of a Cys having conventional N^{α} or S^{β} protection, e.g. Brik et al, J. Org. Chem., 65: 3829-3835 (2000).

Peptide synthesis

Solid-phase synthesis is performed on a custom–modified 433A peptide synthesizer from Applied Biosystems, using in situ neutralization/2-(1H-benzotriazol-1-yl)-1,1,1,3,3-tetramethyluronium hexafluoro-phosphate (HBTU) activation protocols for stepwise Boc chemistry chain elongation, as described by Schnolzer et al, Int. J. Peptide Protein Res., 40: 180-193 (1992). Each synthetic cycle consists of N^{α}-Boc –removal by a 1 to 2 min treatment with neat TFA, a 1-min DMF flow wash, a 10-min coupling time with 2.0 mmol of preactivated Boc-amino acid in the presence of excess DIEA and a second DMF flow wash. Nα-Boc-amino acids (2 mmol) are preactivated for 3min with 1.8mmol HBTU (0.5M in DMF) in the presence of excess DIEA (6mmol). After coupling of Gln residues, a dichloromethane flow wash is used before and after deprotection using TFA, to prevent possible high temperature (TFA/DMF)–catalyzed pyrrolidone carboxylic acid formation. Side-chain protected amino acids are Boc-Arg(p-toluenesulfonyl)-OH, Boc-Asn(xanthyl)-OH, Boc-Asp(O-cyclohexyl)-OH, Boc-Cys(4-methylbenzyl)-OH, Boc-Glu(O-cyclohexyl)-OH, Boc-His(dinitrophenylbenzyl)-OH, Boc-Lys(2-Cl-Z)-OH, Boc-Ser(benzyl)-OH, Boc-Thr(benzyl)-OH, Boc-Trp(cyclohexylcarbonyl)-OH and Boc-Tyr(2-Br-Z)-OH (Orpagen Pharma, Heidelberg, Germany). Other amino acids are used without side chain protection. C-terminal Fragment 1 is synthesized on Boc-Leu-O-CH_2-Pam resin (0.71mmol/g of loaded resin), while for Fragments 2 through 5 machine-assisted synthesis is started on the Boc-Xaa-S-CH_2-CO-Leu-Pam resin. This resin is obtained by the coupling of S-acetylthioglycolic acid pentafluorophenylester to a Leu-PAM resin under standard conditions. The resulting resin is used as a starting resin for peptide chain elongation on a 0.2 mmol scale after removal of the acetyl protecting group with a 30min treatment with 10% mercaptoethanol, 10% piperidine in DMF.

After chain assembly is completed, the peptide fragments are deprotected and cleaved from the resin by treatment with anhydrous hydrogen fluoride for 1hr at 0°C with 5% p-cresol as a scavenger. In all cases except Fragment 1, the imidazole side chain 2,4-dinitrophenyl (DNP) protecting groups remain on His residues because the DNP-removal procedure is incompatible with C-terminal thioester groups. However DNP is gradually removed by thiols during the ligation

reaction, yielding unprotected His. After cleavage, peptide fragments are precipitated with ice–cold diethylether, dissolved in aqueous acetonitrile and lyophilized. The peptide fragments are purified by RP-HPLC with a C18 column from Waters by using linear gradients of buffer B (acetonitile/0.1% trifluoroacetic acid) in buffer A (H_2O/0.1% trifluoroacetic acid) and UV detection at 214nm. Samples are analyzed by electrospray mass spectrometry (ESMS) using an Esquire instrument (Brücker, Bremen , Germany), or like instrument.

Native chemical ligations

As described more fully below, the ligation of unprotected fragments is performed as follows: the dry peptides are dissolved in equimolar amounts in 6M guanidine hydrochloride (GuHCl), 0.2M phosphate, pH 7.5 in order to get a final peptide concentration of 1-8 mM at a pH around 7, and 1% benzylmercaptan, 1% thiophenol is added. Usually, the reaction is carried out overnight and is monitored by HPLC and electrospray mass spectrometry. The ligation product is subsequently treated to remove protecting groups still present. Opening of the N-terminal thiazolidine ring further required the addition of solid methoxamine to a 0.5M final concentration at pH3.5 and a further incubation for 2h at 37°C. A 10-fold excess of Tris(2-carboxyethyl)phosphine is added before preparative HPLC purification. Fractions containing the polypeptide chain are identified by ESMS, pooled and lyophilized.

The ligation of fragments 4 and 5 is performed at pH7.0 in 6 M GuHCl. The concentration of each reactant is 8mM, and 1% benzylmercaptan and 1% thiophenol were added to create a reducing environment and to facilitate the ligation reaction. An almost quantitative ligation reaction is observed after overnight stirring at 37°C. At this point in the reaction, CH_3-O-NH_2.HCl is added to the solution to get a 0.5M final concentration, and the pH adjusted to 3.5 in order to open the N-terminal thiazolidine ring. After 2h incubation at 37°C, ESMS is used to confirm the completion of the reaction. The reaction mixture is subsequently treated with a 10-fold excess of Tris(2-carboxyethylphosphine) over the peptide fragment and after 15min, the ligation product is purified using the preparative HPLC (e.g., C4, 20-60% CH_3CN, 0.5% per min), lyophilized, and stored at –20°C.

The same procedure is repeated for the remaining ligations with slight modifications.

Polypeptide Folding

The full length peptide is refolded by air oxidation by dissolving the reduced lyophilized protein (about 0.1 mg/mL) in 1M GuHCl, 100mM Tris, 10mM methionine, pH 8.6 After gentle stirring overnight, the protein solution is purified by RP-HPLC as described above.

Example 3: Preparation of HPP antibody compositions

Substantially pure HPP or a portion thereof is obtained. The concentration of protein in the final preparation is adjusted, for example, by concentration on an Amicon filter device, to the level of a few micrograms per ml. Monoclonal or polyclonal antibodies to the protein are then prepared as described in the sections titled "Monoclonal antibodies" and "Polyclonal antibodies."

Briefly, to produce an anti-HPP monoclonal antibody, a mouse is repetitively inoculated with a few micrograms of the HPP or a portion thereof over a period of a few weeks. The mouse is then sacrificed, and the antibody producing cells of the spleen isolated. The spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells destroyed by growth of the system on selective media comprising aminopterin (HAT media). The successfully fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as ELISA, as originally described by Engvall, E., Meth. Enzymol. 70: 419 (1980). Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis, L. et al. Basic Methods in Molecular Biology Elsevier, New York. Section 21-2.

For polyclonal antibody production by immunization, polyclonal antiserum containing antibodies to heterogeneous epitopes in the HPP or a portion thereof are prepared by immunizing a mouse with the HPP or a portion thereof, which can be unmodified or modified to enhance immunogenicity. Any suitable nonhuman animal, preferably a non-human mammal, may be selected including rat, rabbit, goat, or horse.

Antibody preparations prepared according to either the monoclonal or the polyclonal protocol are useful in quantitative immunoassays which determine concentrations of HPP in biological samples; or they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies may also be used in therapeutic compositions for killing cells expressing the protein or reducing the levels of the protein in the body.

Example 4: Characterisation of HPP polypeptides in vivo

The mouse homologous/orthologuous proteins of the HPP polypeptides are administered subcutaneously to male C57BL/6 mice for 7 to 14 days at a dose of 300, 600 or 1000 microg/day. At the end of the treatment period samples from all organs are subjected to snap freezing at necropsy and are analyzed with GeneChip® expression profiling.

Total RNA is extracted from these frozen tissues using TRIzol reagent (Life Technologies) according to the manufacturer's instructions. Total RNA is quantified by the absorbance at $\lambda = 260$ nm (A260nm), and the purity is estimated by the ratio A260nm/A280nm. Integrity is checked by denaturing gel electrophoresis. RNA is stored at -80°C until analysis. Good quality total RNA is used to synthesize double-stranded cDNA using the Superscript Choice System (Life Technologies). The cDNA is then in vitro transcribed (MEGAscript™ T7 Kit, Ambion) to form biotin labeled cRNA. Next, 12 to 15 mg of labeled cRNA is hybridized to the Affymetrix Mouse MOE430A expression probe arrays for 16 hours at 45°C. Arrays are then washed according to the EukGE-WS2 protocol (Affymetrix), and stained with 10 mg/ml of streptavidin-phycoerythrin conjugate (Molecular Probes). The signal is antibody-amplified with 2 mg/ml acetylated BSA (Life Technologies), 100 mM MES, 1 M [Na+], 0.05 % Tween 20, 0.005 % Antiofoam (Sigma), 0.1mg/ml goat IgG and 0.5 mg/ml biotinylated antibody and re-stained with the streptavidin solution. After washing, the arrays are scanned twice with the Gene Array® scanner (Affymetrix).

The expression level is estimated by averaging the differences in signal intensity measured by oligonucleotide pairs of a given probe (AvgDiff value). The image acquisition and numerical translation software used for this study is the Affymetrix Microarray Suite version 5 (MAS5). To identify genes that are impacted by treatment, the dataset is initially filtered to exclude in a first wave of analysis genes whose values are systematically in the lower expression ranges where the experimental noise is high (at least an AvgDiff value of 50 in a number of experiments corresponding to the smallest number of replicas of any experimental point). In a second round of selection a threshold t-test p-value (0.05) identifies genes with different values between treated and non-treated based on a two component error model (Global Error Model) and, where possible, with a stepdown correction for multi-hypothesis testing (Benjamini and Hochberg false discovery rate).

The selected genelists are then compared with established genelists for pathways and cellular components using Fisher's exact test. Venn diagrams are used to identify the gene changes that are in common between the different organs. Expression profiles of highly relevant genes are used to find genes with correlated changes at individual experimental points, using several distance metrics (standard, Pearson).

The decision to consider a specific gene relevant is based on a conjunction of numerical changes identified by exploratory filtering and statistical algorithms as described above and the relationship to other modulated genes that point to a common biological theme.

Tables 4 and 6 to 11 shows that at the RNA level HPP polypeptides affect genes that are related to apoptosis pathway, proteosome, ubiquitin pathways and ribosomal RNAs and proteins. Most genes

are up-regulated more than at least 1.2 fold or down-regulated at least less than 0.8 fold.

4.1: Characterisation of HPP-38 polypeptide in vivo

HPP-38 polypeptide was administered to mice, the expression level was estimated and a genelist was selected as described above (Table 4).

Table 4

Fold-change	Gene Title	Gene Symbol
0.8	Bag3	Bcl2-associated athanogene 3
1.6	Cebpb	CCAAT/enhancer binding protein (C/EBP), beta
1.2	Prdx2	peroxiredoxin 2
1.5	Cfdp	craniofacial development protein 1
1.2	Dsip1	delta sleep inducing peptide, immunoreactor
1.2	Bnip3	BCL2/adenovirus E1B 19kDa-interacting protein 1, NIP3
1.3	Tia1	cytotoxic granule-associated RNA binding protein 1
1.1	Card10	caspase recruitment domain family, member 10
1.5	Bcl2l1	Bcl2-like 1
1.5	Tegt	testis enhanced gene transcript
1.1	Dedd2	death effector domain-containing DNA binding protein 2
2.3	Dnase1	deoxyribonuclease I
2.4	Dnase2a	deoxyribonuclease II alpha
1.4	Bag1	Bcl2-associated athanogene 1
0.7	Plagl1	pleiomorphic adenoma gene-like 1
1.4	Ebag9	estrogen receptor-binding fragment-associated gene 9
1.2	Tnfrsf21	tumor necrosis factor receptor superfamily, member 21
1.4	Dap3	death associated protein 3
1.5	Sh3glb1	SH3-domain GRB2-like B1 (endophilin)

An in vitro experiment on 15 tumor cell lines was done. The assay used to detect changes in cell proliferation was based on the ability of viable cells to cause alamarBlue to change from its oxidized non-fluorescent blue form to a reduced fluorescent red form. With the results obtained from the alamarBlue reaction, cell proliferation can be quantified and metabolic activity of viable cells examined. The test compound was dissolved and diluted with sterile distilled water to obtain an initial

working solutions of 10000, 1000, 100, 10 and 1 micromolar. A 100-fold dilution was further made in culture media to generate the final assay concentrations of 100, 10, 1, 0.1 and 0.01 micromolar. Aliquotes of 100 microliter of cell suspension (about 1500 – 5000 cell per well) were placed in 96-well microtiter plates in an atmosphere of 5% carbon dioxide at 37 degrees celsius. After 24 hours, 100 microliters of growth medium and 2 microliters of test solution, mitomycin (positive control substance) or vehicle (distilled water), were added repectively per well in duplicate for an additional 72-hour incubation. The test substance was evaluated for possible inhibitory effect on cell proliferation at concentrations of 100, 10, 1, 0.1 and 0.01 micromolar. At the end of incubation,20 microliters of 90% alamarBlue reagent was added to each well for another 6 hour incubation before detection of cell viability by fluorescent intensity. Fluorescent intensity was measured using Spectafluor Plus plate reader with extinction at 530 nm and emission at 590 nm. A decrease of 50% or more in fluorescent intensity relative to vehicle-treated control cultures indicated significant cell growth inhibition, cytostatic or cytotoxic activity and a semi-quantitative IC50, TBI and LC50 were then determined by nonlinear regression analysis). The results showed that at least some tumor cell lines were more susceptible to HPP-38 induced cytotoxicity or inhibition of cell growth than other tumor cell lines. Therefore, HPP-38 has some selectivity. These results demonstrate the potential of HPP-38 as an anti-cancer agent.

Table 5:

Assay	[a]IC_{50}	[b]TGI	[c]LC_{50}
Tumor, Breast, MCF-7	76 μM	> 100 μM	> 100 μM
Tumor, Colon, DLD-1	56 μM	> 100 μM	> 100 μM
Tumor, Kidney, A-498	31 μM	> 100 μM	> 100 μM
Tumor, Leukemia, K562	> 100 μM	> 100 μM	> 100 μM
Tumor, Liver, HepG2	45 μM	> 100 μM	> 100 μM
Tumor, Lung, A549	72 μM	> 100 μM	> 100 μM
Tumor, Lymphoma, H33HJ-JA1	> 100 μM	> 100 μM	> 100 μM
Tumor, Melanoma, SK-MEL-5	85 μM	> 100 μM	> 100 μM
Tumor, Neuroepithelioma, SK-N-MC	9.5 μM	> 100 μM	> 100 μM
Tumor, Ovary, OVCAR-3	> 100 μM	> 100 μM	> 100 μM
Tumor, Pancreas, PANC-1	29 μM	> 100 μM	> 100 μM

Tumor, Prostate, PC-3	10 μM	> 100 μM	> 100 μM
Tumor, Skin, A431	15 μM	> 100 μM	> 100 μM
Tumor, Stomach, KATO III	> 100 μM	> 100 μM	> 100 μM
Tumor, Uterus, MES-SA	16 μM	> 100 μM	> 100 μM

[a]IC_{50} (50% Inhibition Concentration): Test compound concentration where the increase from $time_0$ in the number or mass of treated cells was only 50% as much as the corresponding increase in the vehicle-control at the end of experiment.
[b]TGI (Total Growth Inhibition): Test compound concentration where the number or mass of treated cells at the end of experiment was equal to that at $time_0$.
[c]LC_{50} (50% Lethal Concentration): Test compound concentration where the number or mass of treated cells at the end of experiment was half that at $time_0$.
A semi-quantitative determination of IC_{50}, TGI and LC_{50} was carried out by nonlinear regression analysis using GraphPad Prism (GraphPad Software, USA).

4.2: Characterisation of HPP-13 polypeptides in vivo

HPP-13 polypeptide was administered to mice, the expression level was estimated and a genelist was selected as described above (Tables 6, 7, 8, 9 and 10). Genes affected are related to iron transport, iron metabolism, heme biosynthesis, erythropoiesis and immune-regulation or related to neurodegeneration (Table 11). The fold-changes are either greater than or less than 1.2.

Table 6: Erythropoiesis genes

Fold-change	Gene Symbol	Gene Title
2.7	Ermap	erythroblast membrane-associated protein
1.5	Epb4.1	erythrocyte protein band 4.1
1.0	Epb4.1l3	erythrocyte protein band 4.1-like 3
3.6	Epb4.2	erythrocyte protein band 4.2
3.3	Epb4.2	erythrocyte protein band 4.2
2.2	Epb4.9	erythrocyte protein band 4.9
2.0	Epb7.2	erythrocyte protein band 7.2
1.6	Epb7.2	erythrocyte protein band 7.2
1.6	Epb7.2	erythrocyte protein band 7.2
1.6	Epb7.2	erythrocyte protein band 7.2
1.6	Epb7.2	erythrocyte protein band 7.2

2.1	Eraf	erythroid associated factor
1.5	Epor	erythropoietin receptor
3.0	Gypa	glycophorin A
2.5	Gypa	glycophorin A
2.2	Ank1	ankyrin 1, erythroid
1.8	Ank1	ankyrin 1, erythroid
3.0	Ank1	ankyrin 1, erythroid
2.2	Tal 1	T-cell acute lymphatic leukemia 1

Table 7: Iron transport, heme biosynthesis and iron metabolism and erythropoiesis genes

Fold-change	Gene Symbol	Gene Title
3.5	Trfr	transferrin receptor
1.1	Trfr2	transferrin receptor 2
1.9	Fech	ferrochelatase
1.7	Lft	lactotransferrin
2.4	Urod	uroporphyrinogen decarboxylase
1.3	Uros	uroporphyrinogen 111 synthase
1.6	Ppox	protoporphyrinogen oxidase
2.8	Nfe2	nuclear factor, erythroid derived 2
2.4	Alad	aminolevulinate, delta-, dehydratase
1.6	Alas2	aminolevulinate acid synthase 2, erythroid

Table 8: Erythropoiesis and immune-related genes

Fold-change	Gene Symbol	Gene Title
0.7	Tnfsf 13b	tumor necrosis factor (ligand) superfamily, member 13b
0.8	Tnfsf 12a	tumor necrosis factor (ligand) superfamily, member 12a
0.8	Tnfsf 13c	tumor necrosis factor (ligand) superfamily, member 13c
0.9	Tnfsf 18	tumor necrosis factor (ligand) superfamily, member 18
0.7	Tnfsf 1b	tumor necrosis factor (ligand) superfamily, member 1b

1.0	Tnfsf 21	tumor necrosis factor (ligand) superfamily, member 21
0.9	Tnfsf 25	tumor necrosis factor (ligand) superfamily, member 25
0.7	Tnfsf 5	tumor necrosis factor (ligand) superfamily, member 5
0.7	Tnfsf 7	tumor necrosis factor (ligand) superfamily, member 7
0.8	Tnfaip 1	tumor necrosis factor, alpha-induced protein 1 (endothelial)
1.5	Tnfaip 2	tumor necrosis factor, alpha-induced protein 2

Table 9: Immune-related genes: T-cell receptor related genes

Fold-change	Gene Symbol	Gene Title
2.2	Tal 1	T-cell acute lymphatic leukemia 1
1.0	Tlx 1	T-cell leukemia, homeobax 1
0.7	Tcra	T-cell receptor alpha chain
0.7	Tcrb-J	T-cell receptor beta, joining region
0.8	Tcrb-V13	T-cell receptor beta, variable 13
0.8	Tcrb-V8.2	T-cell receptor beta, variable 8.2
0.7	Tgtp	T-cell specific GTPase
0.8	Tcirg1	T-cell, immune regulator 1
0.7	Zap70	zeta-chain (TCR) associated protein kinase
0.8	Tccr	T-cell cytokine receptor

Table 10: CD (cluster differentiation)- related genes involved in immune-regulation and hematopoiesis

Fold-change	Gene Symbol	Gene Title
0.7	Cd28	CD28 antigen
0.8	Cd3d	CD3 antigen, delta polypeptide
0.8	Cd3e	CD3 antigen, epsilon polypeptide
0.7	Cd3g	CD3 antigen, gamma polypeptide
0.6	Cd3z	CD3 antigen, zeta polypeptide
0.6	Cd8a	CD8 antigen, alpha polypeptide
0.8	Cd8b	CD8 antigen, beta polypeptide
0.7	Cd22	CD22 antigen

1.6	Cd24a	CD24a antigen
1.4	Cd36	CD36 antigen
1.9	Cd59a	CD59a antigen

Table 11:Genes related to Neurodegeneration

Fold change	Gene Title	Gene symbol
0.4	Ptpn11	protein tyrosine phosphatase, non-receptor type 11
0.5	Cited2	Cbp/p300-interacting transactivator 2
0.5	Mef2c	myocyte enhancer factor 2C
0.5	Cdh5	cadherin 5
1.8	Sema4g	semaphorin 4G
1.8	Hmgcr	3-hydroxy-3-methylglutaryl-Coenzyme A reductase
2.0	Dtna	dystrobrevin alpha
2.0	S100b	S100 protein, beta polypeptide, neural
2.0	Fbxo23	F-box only protein 23
2.0	Ank3	ankyrin 3, epithelial
2.1	Etv1	ets variant gene 1
2.1	Sema5a	semaphorin 5A
2.2	Hmgcs1	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1
2.2	Cdh2	cadherin 2
2.3	Dmd	dystrophin, muscular dystrophy
2.4	Cdh1	cadherin 1
2.4	Mt3	metallothionein 3
2.8	Plp	proteolipid protein (myelin)

4.3: Characterisation of HPP-23 polypeptide in vivo

HPP-23 was administered to mice, the expression level was estimated and a genelist was selected as described above (Table 12). Genes affected are related to sugar metabolism (e.g glucose), angiogenesis, vasculogenesis, blood pressure.

Table 12

Fold-change	Gene Symbol	Gene Title
1.6	Fiz1	Flt3 interacting zinc finger protein 1
1.3	Flt3	FMS-like tyrosine kinase 3

2.1	Aamp	angio-associated migratory protein
1.9	Angptl4	angiopoietin-like 4
0.4	Atm	ataxia telangiectasia mutated homolog (human)
1.6	Adra2a	adrenergic receptor, alpha 2a
1.3	Ace	angiotensin converting enzyme
0.6	Epha4	Eph receptor A4
0.7	Epha6	Eph receptor A6
1.5	Efna3	ephrin A3
0.5	Vegfa	vascular endothelial growth factor A
1.3	Vegfb	vascular endothelial growth factor B
2.0	Egfl7	vascular endothelial zinc finger 1
0.7	Tbc1d8	vascular Rab-GAP/TBC-containing
1.3	Vasp	vasodilator-stimulated phosphoprotein
1.5	Adcyap1r1	adenylate cyclase activating polypeptide 1 receptor 1
1.9	Avp	arginine vasopressin
1.5	Evl	Ena-vasodilator stimulated phosphoprotein
1.3	Fibp	fibroblast growth factor (acidic) intracellular binding protein
1.5	Fgf13	fibroblast growth factor 13
0.6	Fgfr2	fibroblast growth factor receptor 2
2.4	Fgfrl1	fibroblast growth factor receptor-like 1

4.4: Characterisation of HPP-13 and GPA101 polypeptides in vivo

4.4.1. Introduction

Progressive cell loss in neuronal populations is a pathological hallmark of neurodegenerative diseases. Discovery of neurotrophins such as NGF (nerve growth factor), BDNF (brain-derived neurotrophic factor), NT-3 (neurotrophin 3), NT-4/5 (neurotrophin 4/5) or GDNF (glial cell line-derived neurotrophic factor) open a large and promising investigation field. Neurotrophic factors have been used for the treatment of several neurodegenerative diseases. However, their use is limited by their inability to cross the blood-brain barrier, their short half life and their side effects. So, the development of new compounds which could mimic neurotrophins effects (promoting neuron survival and neurite outgrowth) without their limitation appears to be a good strategy for the development of

new therapeutics in neurodegenerative diseases.

The purpose of the present in-vitro study is to investigate the putative neurotrophic effects of HPP-13 and GPA101 on neurite outgrowth from spinal motor neuron. The neurotrophic effect of test compounds are investigated 3 days after treatment by measuring the length of the major neurite. Two cultures are done and two Petri dishes per conditions are performed.

4.4.2. Materials and Methods

4.4.2.1 Motor neurons culture

Rat spinal motor neurons are prepared according to the method described by Martinou et al. (1992) Neuron, 8, 737-744.. Briefly, pregnant female rats of 15 days gestation are killed by cervical dislocation (Rats Wistar; Janvier, Le Genest-St-Isle, France) and the fetuses are removed from the uterus. Their spinal cords are removed and placed in ice-cold medium of Leibovitz (L15, Gibco, Invitrogen, Cergy-Pontoise, France). Meninges are carefully removed. Spinal cord tissue is dissociated by trypsinization (trypsin, Gibco) for 30 min at 37°C in the presence of DNAase I (Roche Meylan). The reaction is stopped by addition of DMEM containing 10% fetal bovine serum (Gibco). The suspension is triturated with a 10 ml pipette and cells are then mechanically dissociated by several passages through the 21-gauge needle of a syringe. Cells are then centrifuged at 580 x g for 10 min at room temperature. The pellet of dissociated cells is resuspended in L15 medium and the resulting suspension is first enriched in motor neurons by centrifugation for 10 min at 180 x g for 10 min at room temperature on a layer of 3.5 % solution of bovine serum albumin (BSA) in L15 medium. The supernatant is discarded, the pellet is homogenized in L15 supplemented with DNAase I, the suspension is layered over a cushion of Optiprep (d: 1.06 g.mL-1; Abcys, Paris, France) and centrifuged at 335 x g for 15 min at room temperature. The upper phase, containing the purified motor neurons, is collected, resuspended in L15, centrifuged at 800 x g for 10 min at room temperature. The cell pellet is finally resuspended in a defined culture medium consisting of Neurobasal (Gibco) supplemented with B27 supplement (2%; Gibco) and 0.5 mM of L-Glutamine (Gibco). This culture medium does not contain any serum: Neurobasal is a serum-free medium for long-term viability neurons but formulation is confidential (official data sheet is available on invitrogen website); B27 is a supplement added to give the optimal growth condition (B27 supplement contains following constituents: d-Biotin, BSA, fatty acid free Fraction V, Catalase, L-Carnitine HCl, Corticosterone, Ethanolamine HCl, D-Galactose (Anhyd.), Glutathione (Reduced), Insulin (Human, Recombinant), Linoleic Acid, Linolenic Acid, Progesterone, Putrescine.2HCl, Sodium Selenite (1000X), Superoxide

Dismutase, T-3/Albumin Complex, DL Alpha-Tocopherol, DL Alpha Tocopherol Acetate Transferrin (Human, Iron-Poor), Vitamin A Acetate). Viable cells are counted in a Neubauer cytometer using the trypan blue exclusion test (Sigma). Then cells are plated at 30 000 cells per Petri dish (Nunc, Dutscher, pre-coated with poly-l-lysine) and cultured at 37°C in a humidified air (95%) – CO2 (5%) atmosphere. Two hours after plating (time needed for cell adhesion), tested compounds are added on culture.

This study employed the following conditions:

- Control
- + BDNF at 50 ng/ml
- + HPP-13 (SEQ ID No: 393) at 1 nM
- + HPP-13 (SEQ ID No: 393) at 10 nM
- + HPP-13 (SEQ ID No: 393) at 30 nM
- + GPA101 at 1 nM
- + GPA101 at 10 nM
- + GPA101 at 30 nM

4.4.2.2 Evaluation of neurite outgrowth

After 3 days of treatment, the cultures are washed in phosphate-buffered saline (PBS, Gibco) and fixed in glutaraldehyde 2.5% in PBS. 80 to 100 pictures of cells with neurites without any branching are taken per condition (approximately half on each dish) with a camera (Coolpix 995 ;Nikon) fixed on microscope (Nikon, objective 20x) and the length measurement are made by analysis of pictures by software (Image-Pro Plus, France).

4.4.2.3 Data analysis

A global analysis of the data is done using a one way analysis of variance (ANOVA). Where applicable, Fisher's PLSD test is used for multiple pairwise comparisons. The level of significance was set at $p < 0.05$.

4.4.3 Results

4.4.3.1 Effect of BDNF

BDNF tested at 50 ng/ml induced a neuritic outgrowth on spinal motor neuron. In control condition after 3 days of culture, the principal neurite length was about 111.74 µm ± 4.032 whereas with BDNF,

the principal neurite reached 199.56 µm ± 7.122. An increase of 77% was observed.

Table 13:

	Neurite Outgrowth (% of control)	sem
Control (n=96)	100.00	3.012
BDNF 50 ng/ml (n=82)	177.79	5.169
HPP-13 (SEQ ID No: 393) 1 nM (n=94)	160.41	4.795
HPP-13 (SEQ ID No: 393) 10 nM (n=91)	172.70	6.582
HPP-13 (SEQ ID No: 393) 30 nM (n=91)	156.79	5.919
GPA101 1 nM (n=102)	138.42	4.486
GPA101 10 nM (n=89)	161.07	6.553
GPA101 30 nM (n=96)	146.85	5.418

4.4.3.2 Effect of HPP-13 and GPA101

HPP-13 and GPA101 also significantly increase neurite outgrowth, the neurite outgrowth is similar to BDNF condition. For each compound the best concentration is found to be 10 nM. For this concentration, the mean neurite length reached 193.65. µm ± 8.737 for HPP-13 and 179.74 µm ± 7.545 for GPA101. For all the test concentrations, the mean neuritic length reaches 150% of control condition.

4.4.4 Discussion

In this study, a large neurotrophic effect of HPP-13 and GPA101 was observed.

Example 4.5: Characterisation of HPP-23 polypeptide in vivo

HPP-23 was administered to mice, the expression level was estimated and a genelist was selected as described above (Table 14). Genes affected are related to sugar amyloidosis, arrhythmia or angiogenesis (e.g. stroke, macular regeneration, cancer).

Table 14:

Fold change	Gene Title	Gene Symbol
0.8	Notch2	Notch gene homolog 2 (Drosophila)
1.3	Notch3	Notch gene homolog 3 (Drosophila)
1.4	Notch4	Notch gene homolog 4 (Drosophila)
1.7	Numbl	numb-like
1.3	Snai1	snail homolog 1 (Drosophila)
0.8	Adam17	---

1.3	Psen1	presenilin 1
1.5	Psen2	presenilin 2
0.5	Ryr2	ryanodine receptor 2, cardiac
0.8	Trdn	triadin
0.8	Calm2	calmodulin 2
0.8	Frap1	FK506 binding protein 12-rapamycin associated protein 1
2.4	Ppp1ca	protein phosphatase 1, catalytic subunit, alpha isoform
1.3	Ppp1cb	protein phosphatase 1, catalytic subunit, beta isoform
1.8	Ppp1r11	protein phosphatase 1, regulatory (inhibitor) subunit 11
1.8	Ppp1r14a	protein phosphatase 1, regulatory (inhibitor) subunit 14A
1.7	Ppp1r1a	protein phosphatase 1, regulatory (inhibitor) subunit 1A
0.8	Ppp1r7	protein phosphatase 1, regulatory (inhibitor) subunit 7
1.3	Rsn	restin
0.8	2210417O06Rik	RIKEN cDNA 2210417O06 gene (sorcin)
1.5	Hes1	hairy and enhancer of split 1 (Drosophila)
0.8	Vegfa	vascular endothelial growth factor A
2.1	Aamp	angio-associated migratory protein
1.4	Amot	angiomotin
1.3	Angptl2	angiopoietin-like 2
2.0	Angptl4	angiopoietin-like 4
1.3	Ace	angiotensin converting enzyme
1.8	Apoe	apolipoprotein E
1.9	Tbca	tubulin cofactor a
1.4	Tuba1	tubulin, alpha 1
1.7	Tuba1	tubulin, alpha 1
1.6	Tuba4	tubulin, alpha 4
1.8	Tubb3	tubulin, beta 3
1.5	Tubb4	tubulin, beta 4
2.0	Tubb5	tubulin, beta 5
1.5	Tbcd	tubulin-specific chaperone d
1.2	Bbp	beta-amyloid binding protein precursor
1.2	D130054N24Rik	beta-site APP cleaving enzyme
1.3	App	amyloid beta (A4) precursor protein
1.2	Apba2	amyloid beta (A4) precursor protein-binding, family A, member 2
2.3	Apba3	amyloid beta (A4) precursor protein-binding, family A, member 3
2.2	Apbb1	amyloid beta (A4) precursor protein-binding, family B, member 1
0.8	Apbb2	amyloid beta (A4) precursor protein-binding, family B, member 2

0.8	Apbb3	amyloid beta (A4) precursor protein-binding, family B, member 3
1.7	Aplp1	amyloid beta (A4) precursor-like protein 1
1.3	Aplp2	amyloid beta (A4) precursor-like protein 2
1.8	Appbp2	amyloid beta precursor protein (cytoplasmic tail) binding protein 2
1.3	Cox7a2l	cytochrome c oxidase subunit VIIa polypeptide 2-like
1.9	Cox4i1	cytochrome c oxidase, subunit IVa
1.6	Cox6a1	cytochrome c oxidase, subunit VI a, polypeptide 1
0.6	Cox6c	cytochrome c oxidase, subunit VIc
1.7	Cox7a2	cytochrome c oxidase, subunit VIIa 2
1.5	Cox7c	cytochrome c oxidase, subunit VIIc
1.6	Cox8a	cytochrome c oxidase, subunit VIIIa
1.5	Cycs	cytochrome c, somatic
1.7	Cyc1	cytochrome c-1
1.4	Ndufa1	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 1
1.2	Ndufa2	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 2
1.8	Ndufa3	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 3
1.2	Ndufa4	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 4
1.3	Ndufa5	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 5
1.8	Ndufa7	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 7 (B14.5a)
1.5	Ndufa8	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 8
1.4	Ndufa9	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 9
1.7	Ndufb10	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 10
2.2	Ndufb7	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 7
1.9	Ndufb9	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 9
1.8	Ndufc1	NADH dehydrogenase (ubiquinone) 1, subcomplex unknown, 1
1.4	Ndufs2	NADH dehydrogenase (ubiquinone) Fe-S protein 2
1.7	Ndufs4	NADH dehydrogenase (ubiquinone) Fe-S protein 4
1.7	Ndufs5	NADH dehydrogenase (ubiquinone) Fe-S protein 5
2.2	Ndufv1	NADH dehydrogenase (ubiquinone) flavoprotein 1
1.3	Ndufv2	NADH dehydrogenase (ubiquinone) flavoprotein 2
1.4	Pxr1	peroxin 5
1.8	Prdx1	peroxiredoxin 1
1.6	Prdx2	peroxiredoxin 2
1.6	Prdx4	peroxiredoxin 4
1.6	Prdx5	peroxiredoxin 5
1.4	Prdx6	peroxiredoxin 6
1.7	Pte1	peroxisomal acyl-CoA thioesterase 1

1.5	Pex11a	peroxisomal biogenesis factor 11a
1.7	Pex14	peroxisomal biogenesis factor 14
4.6	Pex6	peroxisomal biogenesis factor 6
1.9	Pxf	peroxisomal farnesylated protein
1.3	Pipox	peroxisomal sarcosine oxidase
2.3	Pex16	peroxisome biogenesis factor 16

Example 5: Alignments of human and mouse orthologous peptides

The proteins which were detected in accordance with the present invention in to be present in the human plasma were were searched for homologous mouse sequences suitable for injection into mice as described in Example 4:

Underline denotes peptide sequence used for synthesis

GPA056 (HPP-38)

```
Alignment for Geneprot ID: GP_1727089
Description: esophagus cancer related gene 2
Gene Symbol: ECG2
Identity:    26/74 = 35%
Orthology:   Celera syntenic ortholog

hCP1774830      ---------MKITGG--------LLLLCTVVY-------FCSSSEAASLSPK----KVDC
mCP77316        GGIFRQHLRTSFHGNTKRKKKMVKYFQCSVLFSIMLHLVILAAPGARVWWPTHGLIKIKC
                          .: *.          : *:*::       : ::. *    *.    *:.*

hCP1774830      SIYKK----YPVVAIPCPITYLPVCGSDYITYGNECHLCTESLKSNGRVQFLHDGSC
mCP77316        PYKKVNLSWFNKTVDPCPDLKQPICGTNFVTYDNPCILCVESLKSGGRIRYYYNGRC
                .  *     :  .. ***    *:**::::**.* * **.*****.**::: ::* *
```

GPA065 (HPP-13)

```
Alignment for Geneprot ID: GP_909415
Description: paralog of thymosin, beta 4, X chromosome
Gene Symbol:
Identity:    43/43 = 100%
Orthology:   Novartis mutual best match ortholog, SwissProt ortholog

hCP1740742      ------MSDKPDMAEIEKFDKSKLKKTETQEKNPLPSKETIEQEKQAGES
mCP44000        -------SDKPDMAEIEKFDKSKLKKTETQEKNPLPSKETIEQEKQAGES
                      **********************************************
```

GPA066

```
Alignment for Geneprot ID: GP_909415
Description: paralog of thymosin, beta 4, X chromosome
Gene Symbol:
Identity:    44/44 = 100%
Orthology:   Novartis mutual best match ortholog, SwissProt ortholog

hCP1740742      ------MSDKPDMAEIEKFDKSKLKKTETQEKNPLPSKETIEQEKQAGES
mCP44000        MLLPATMSDKPDMAEIEKFDKSKLKKTETQEKNPLPSKETIEQEKQAGES
                **********************************************
```

GPA068 (HPP-23)

```
Alignment for Geneprot ID: GP_805366
Description: chromogranin A (parathyroid secretory protein 1)
Gene Symbol: CHGA
Identity:    28/52 = 54%
Orthology:   Celera syntenic ortholog

hCP38826        MRSAAVLALLLCAGQVTALPVNSPMNKGDTEVMKCIVEVISDTLSKPSPMPVSQECFETL
mCP7064         MRSTAVLALLLCAGQVFALPVNSPMTKGDTKVMKCVLEVISDSLSKPSPMPVSPECLETL
                ***:************ ********.****:****::*****:********** **:***

hCP38826        RGDERILSILRHQNLLKELQDLALQGAKERAHQ--------------------------
mCP7064         QGDERILSILRHQNLLKELQDLALQGAKERAQQPLKQQQPPKQQQQQQQQQQQQQQQQQQ
                :*******************************:*

hCP38826        QKKHSGFEDELSEVLENQSSQAELKEAVEEPSSKDVMEKREDSKEAEKSG--EATDGARP
mCP7064         EQQHSSFEDELSEVFENQSPDAKHRDAAAEVPSRDTMEKRKDSDKGQQDGFEATTEGPRP
                :::**.********:****.:*: ::*. * .*:*.****:**.:.::.*   :*:*.**

hCP38826        QALPEPMQESKAEGNNQAPGEEEEEEEEATNTHPPASLPSQKYPGPQAEGDSEGLSQGLV
mCP7064         QAFPEPNQESPMMGDSESPGED-----TATNTQSPTSLPSQEHVDPQATGDSE---RGLS
                **:*** ***   *:.::***:      ****:.*:*****:: .*** ****   :**

hCP38826        DREKGLSAEPGWQAKREEEEEEEEEAEAGEEAVPEEEGPTVVLNPHPSLGYKEIRKGESR
mCP7064         AQQQARKAK-----QEEKEEEEEEEAVAREKAGPEE-VPTAASSSHFHAGYKAIQKDDGQ
                 :::. .*:     :.*:******** * *:* ***  **.. ..*   *** *:*.:.:

hCP38826        SEALAVDGAGKPGAEEAQDPEGKGEQEHSQQKEE-EEEMAVVPQGLFR-GGKSGELEQ--
mCP7064         SDSQAVDGDGKTEASEALPSEGKGELEHSQQEEDGEEAMVGTPQGLFPQGGKGRELEHKQ
                *:: **** **. *.**  .***** *****:*: ** *. .*****  ***. ***:
```

```
hCP38826        -----EEERLSKEWEDSKRWSKMDQLAKELTAEKRLEGQEEEEDNRDSSMKLSFRARAYG
mCP7064         EEEEEEEERLSREWED-KRWSRMDQLAKELTAEKRLEG----EDDPDRSMKLSFRTRAYG
                     ******:***** ****:*****************     **: * *******:*****

hCP38826        FRGPGPQLRRGWRPSSREDSLEAGLPLQVRGYPEEKKEEEGSANRRPEDQELESLSAIEA
mCP7064         FRDPGPQLRRGWRPSSREDSVEA------RSDFEEKKEEEGSANRRAEDQELESLSAIEA
                **.******************:**       *.  **************.**************

hCP38826        ELEKVAHQLQALRRG
mCP7064         ELEKVAHQLQALRRG
                ***************
```